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THE BRITISH JOURNAL OF RADIOLOGY

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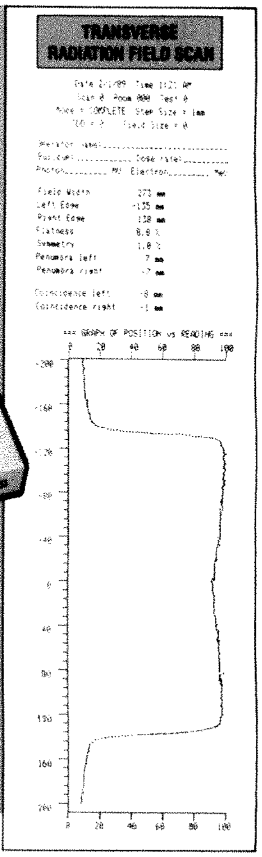

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```
Scan 0  Room 000  Test 0
Mode = COMPLETE  Step Size = 1mm

Field Width          273 mm
Left Edge           -135 mm
Right Edge           138 mm
Flatness             8.9 %
Symmetry             1.8 %
Penumbra left          7 mm
Penumbra right        -7 mm

Coincidence left      -8 mm
Coincidence right     -1 mm

*** GRAPH OF POSITION vs READING ***
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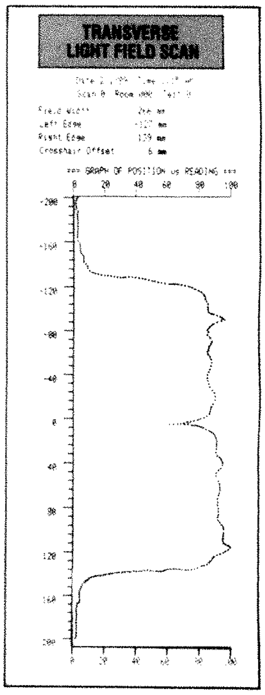
Printed Output of Radiation Field Scan



TRANSVERSE LIGHT FIELD SCAN

```
Field Width          266 mm
Left Edge           -127 mm
Right Edge           139 mm
Crosshair Offset       6 mm

*** GRAPH OF POSITION vs READING ***
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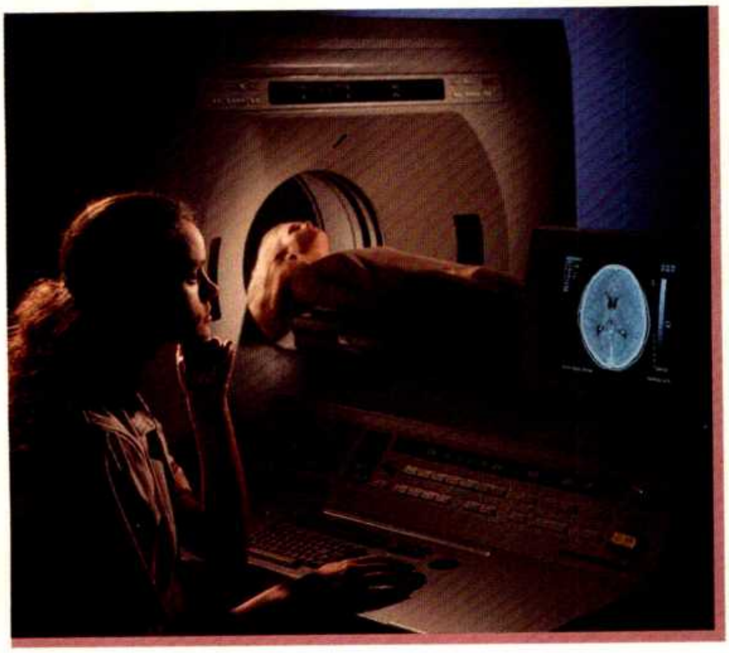

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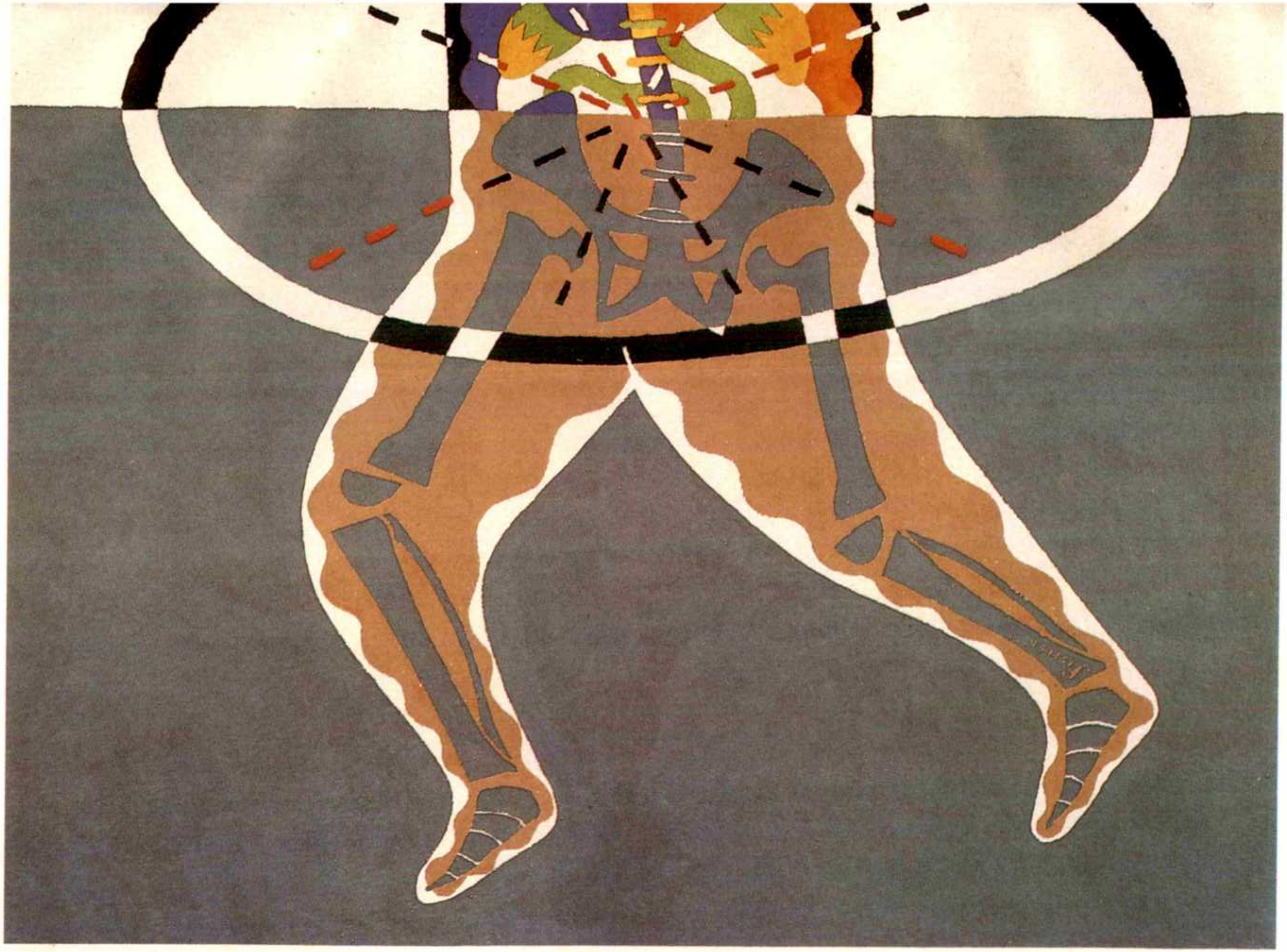

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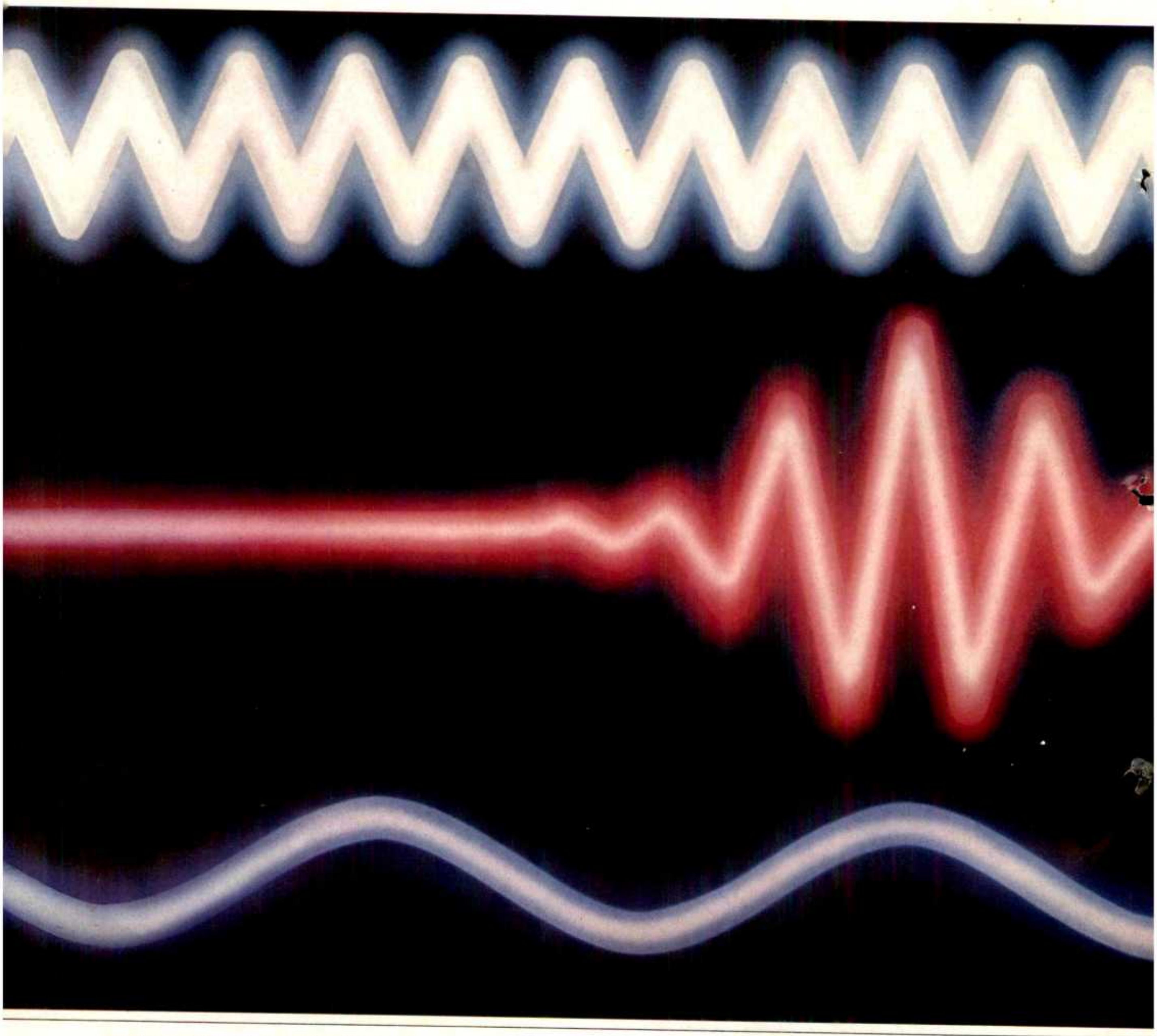

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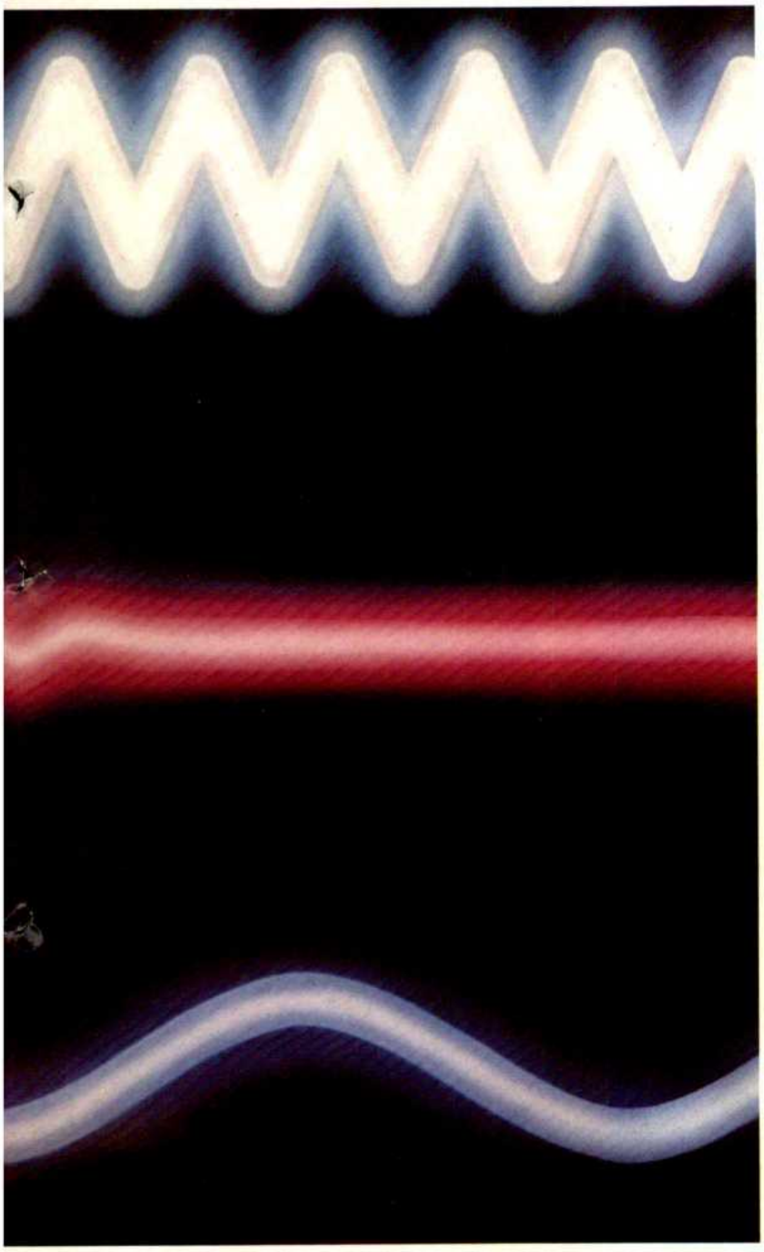

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References: 1. Data on file, Schering Health Care. 2. Kennedy C, et al., (1988), Brit J Radiol; 61:288-293. 3. Wenzel-Hora, B.I., Jahrbuch der Radiologie, (1987). 4. Bryan, R.N. and Hershkowitz N, Invest Radiol, (1984); 19:329-332. 5. Hammer, B. and Knauer, W., Wien Med Wochenschr, (1984); 134(5):113. 6. Stack, J, et al., Neurorad, (1988); 145-154. 7. Hesuftle, M, et al., Radiol, (1988); 167:817-824.

Further information is available from – Schering Health Care, The Brow, Burgess Hill, West Sussex RH15 9NE.

RISKS FROM RADIUM AND THOROTRAST

(BIR Report 21)

Editor

D M Taylor, Kernforschungszentrum, Karlsruhe, Germany

There is long standing concern about the effects in humans of alpha radiation – the induction of cancers, cataracts and kidney damage amongst others.

Information on such risks originate from studies of patients exposed to radium and thorotrast, supplemented and extended by studies of experimental animals.

This volume is the edited proceedings of an international workshop organised by the Commission of the European Communities, the US Department of Energy and the US National Cancer Institute. The workshop is the most recent in a series of meetings reviewing the subject and reflecting the close collaboration between the US and Europe in this area.

Key topics addressed were the epidemiology of radium and thorotrast exposure, dosimetry in exposed persons, clinical and pathological observations, animal data relevant for the extrapolation of human information to other exposure situations, and the assessment of risks from radium, thorotrast or related radionuclides.

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Misinterpretation of the upper parathyroid adenoma on thallium-201/technetium-99m subtraction scintigraphy

By T. Y. K. Chan, FRCS, FRCSEd, *J. W. Serpell, FRACS, O. Chan, FRCS, FRCR,
†J. I. Gaunt, BSc, *A. E. Young, MChir, FRCS and T. O. Nunan, MD, MRCP

Departments of Radiology, *Surgery and †Nuclear Medicine, St Thomas' Hospital, London SE1 7EH

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Keywords: Misinterpretation, Parathyroid, Scintigraphy

Abstract. Pre-operative thallium–technetium subtraction scintigraphy of 50 patients with primary hyperparathyroidism, which was subsequently proven on histology to be due to an adenoma, was compared with operative findings. Six scans were negative and seven uninterpretable. Of the remaining 37 patients, 34 had correct scan prediction of the anatomical locations of the adenomas. On examination of the origins of the adenomas, all six scintigraphic predictions of upper adenomas corresponded to tumours arising from the upper gland found at operation. Of the 25 lower predictions, there was one false positive and 16 were correct, *i.e.* of lower gland origin, but eight were found to originate from the upper gland. This misinterpretation is thought to be due to the prolapse of an adenoma arising from the upper gland towards the lower pole of the thyroid, thereby mimicking a lower lesion on the scan.

Thallium-201/technetium-99m subtraction scintigraphy (TTSS) is an accurate means of localizing parathyroid adenomas pre-operatively. Following its first clinical application by Ferlin et al (1983) and Young et al (1983), Hauty et al (1987) reviewed 14 series and found an overall sensitivity of 82% in localizing abnormal parathyroid tissue; the vast majority of true positives were obtained in patients with adenomas. However, there appear to be difficulties in detecting or localizing adenomas arising from the upper parathyroid gland (Harding et al, 1987; Roses et al, 1989). This study investigates whether this results from misinterpretation on the scan of an adenoma arising from an upper gland as a lower lesion.

Patients and method

The clinical records of all patients who had parathyroid operations by a single surgeon over a 7-year period (1982–1988) were reviewed. The inclusion criteria for the study were:

(1) pre-operative biochemical confirmation of primary hyperparathyroidism (hypercalcaemia with inappropriate level of parathormone);
(2) pre-operative TTSS was performed and the scan results were available for comparison with operative findings; and
(3) the resected specimen was proven on histology to be a parathyroid adenoma.

A total of 50 patients (11 men and 39 women, age range 26–84 years with a mean of 51.5 years) were found to be suitable.

Scanning technique

Double tracer image techniques as described by Young et al (1983) was used in all cases. First, 37 MBq of technetium-99m as pertechnetate was given intravenously to obtain the thyroid image, followed by 80 MBq of thallium-201 in the form of thallous chloride which is taken up by both the thyroid and parathyroid tissues. Data were collected and processed with an on-line computer. Subtraction images were recorded on prints for subsequent analyses.

Surgical exploration

The operation was a standard formal neck exploration to identify and either to excise or to sample for biopsy at least four parathyroid glands in each patient.

Definition

On scintigraphy, an area of increased uptake in the upper half of each hemi-thyroid was taken to indicate an upper adenoma; similarly, increased uptake confined to the lower half of the hemi-thyroid was considered a lower lesion.

At operation, the origin of an adenoma was determined first by the relationship of its vascular pedicle to the poles of the thyroid gland, and, secondly, by the

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Address correspondence to T. Y. K. Chan.

Table I. Analysis of scintigraphic labelling and operative findings

Scintigraphic labelling	Number of patients	Operative findings: origin of adenoma	
		Upper	Lower
Upper	6	6	0
Lower	25*	8 (+1)*	16 (+1)*
Ectopic	3	0	3
Bilateral lower	1	0	1
Unilateral/ indeterminate upper or lower	2	2	0
Normal	6	5	1
Uninterpretable	7	3	4
Total	50	24 (+1)	25 (+1)

*One patient was found to have adenomas originating from both the upper and lower parathyroid glands contralateral to the side of increased uptake on the scan.

presence of an ipsilateral parathyroid gland in either a more superior or inferior position.

Therefore, an area of increased uptake at the lower pole of thyroid on the scan may be considered to be a lower adenoma, but nevertheless found at operation to originate from an upper gland by virtue of the presence of a normal inferior parathyroid gland and of a superior vascular pedicle.

Results

The results are summarized in Table I.

Scintigraphically, six patients had upper pole and 25 had lower pole adenomas. Three patients had increased uptake below the lower pole of the thyroid and were classified as ectopic. One scan showed increased activity in both lower poles, and two scans showed activities spread over the entire hemi-thyroid, making the upper/lower distinction impossible. There were six normal (negative) scans. Seven scans were unsatisfactory or uninterpretable because of movement artefacts or the finding of a nodular thyroid on the pertechnetate scan.

At operation, 24 patients were found to have an adenoma originating from an upper gland, and 25 from a lower gland, the latter including three in the upper thymus which were identified as ectopic on the scans. In addition, one patient was found to have adenomas originating from both upper and lower parathyroid glands contralateral to the side of increased uptake on the scan. The reason for this error is unclear.

Of the six negative ("normal") scans, there were four cases (all of upper gland origin) in which the weight of the adenoma was available; the mean weight was 533 mg (400 mg, 300 mg, 1250 mg and 180 mg) compared with a mean of 1218 mg of 19 positive localizations, in which the weight of the adenoma was also available.

Table II. Operative findings of the eight upper adenomas that were mislabelled as of lower gland origin

Scan prediction	Operative findings (origin of adenoma)	Dimension (cm)	Weight (g)
LL	LU (large, extends to lower pole of thyroid)	4 × 1.5 × 5	2.4
LL	LU (as above)	*	13.2
RL	RU	2 × 1 × 1	1.9
RL	RU	2.5 × 1.5 × 0.7	1.8
LL	LU	3 × 2 × 0.8	1.9
RL	RU	3 × 1 × 0.7	1.3
RL	RU	*	
RL	RU	*	

*Information unavailable.

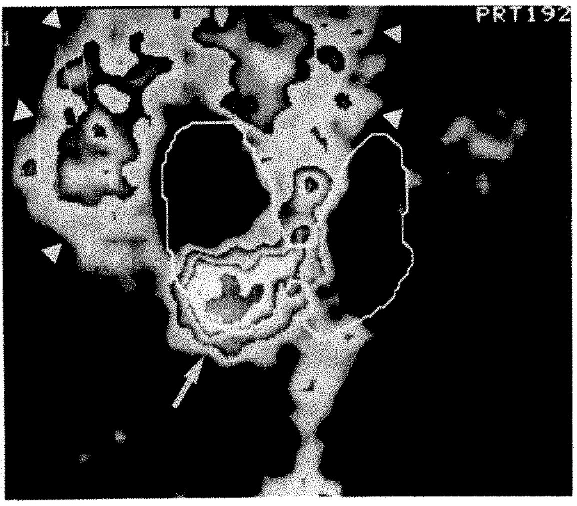
RU: right upper; RL: right lower; LU: left upper; LL: left lower.

Of the eight surgically determined upper adenomas that were labelled as lower lesions on the scan, these were found at operation to be predominantly situated adjacent to the lower pole of the thyroid. Their anatomical locations corresponded to the scan predictions. In an embryological sense, they had been mislabelled, though in the anatomical sense the scan was accurate. The details of the operative findings of these eight adenomas are listed in Table II.

Discussion

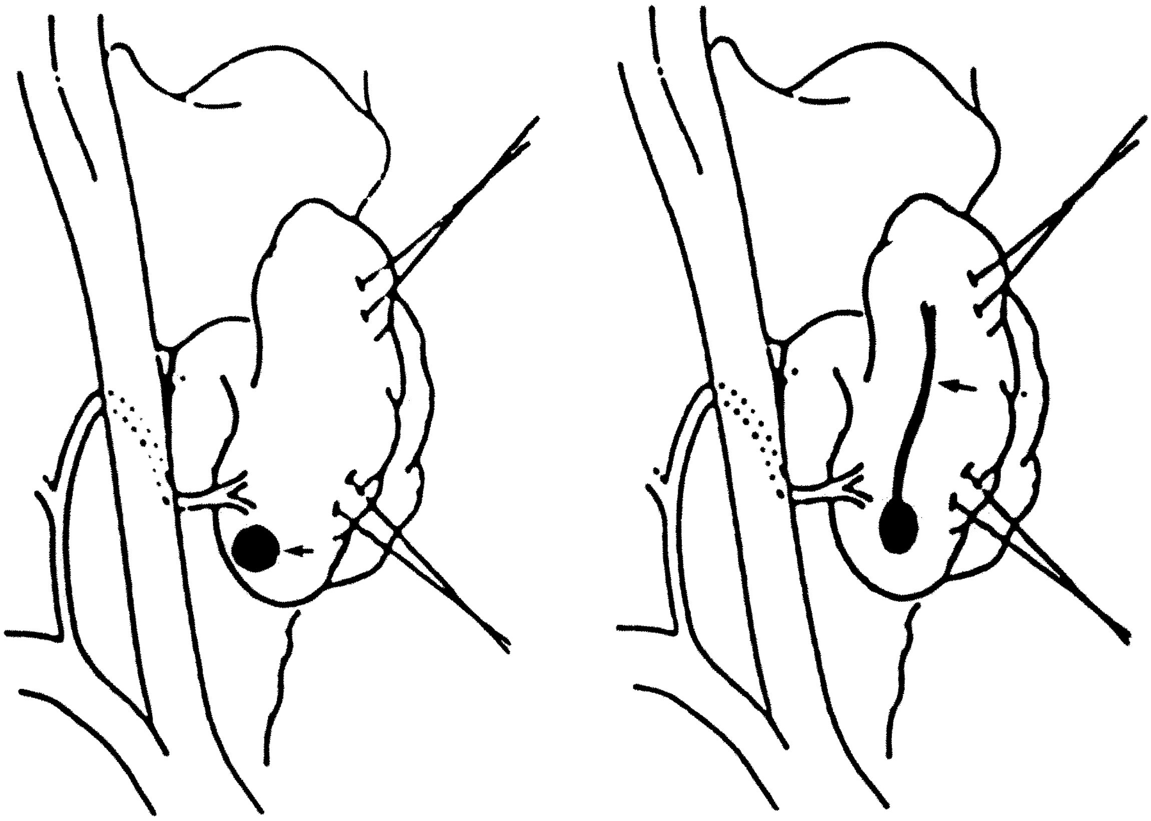
Uptake of thallium by a parathyroid adenoma was first discovered by Fukunaga et al (1979). Ferlin et al (1983) and Young et al (1983) pioneered the clinical application of the subtraction technique, using technetium in addition to thallium. In a review of 14 series, Hauty et al (1987) found an overall sensitivity of 82% for the localization of abnormal parathyroid tissues, the vast majority of true positives being in patients with adenomas. However, there appear to be difficulties in detecting the upper adenoma and it has been postulated that non-visualization of upper adenomas is at least in part due to their deeper cervical location (Harding et al, 1987). Another factor is the small tumour size. Percival et al (1985) indicated that adenomas of less than 600 mg were unlikely to be registered on thallium-201/technetium-99m scintigraphy. The significantly larger size of the adenomas positively localized (mean 1218 mg) on the scan in our series compared with the small size of the negative ones (mean 533 mg) appears to confirm this. The small size and deeper cervical location of these upper adenomas are likely to be the main reasons for their failed detection.

An additional problem with an upper adenoma is the tendency for it to be described as a "lower" lesion on the scan. In other series, three upper adenomas out of a total of 26 adenomas (Percival et al, 1985), three out of eight upper adenomas (Harding et al, 1987) and three of six upper adenomas (Roses et al, 1989) were thought to be lower lesions on the scans. In our series, eight



(a)

Figure 1. Scintigraphic mislabelling of an adenoma arising from the embryologically upper parathyroid gland. (a) Scan prediction of a lower adenoma (arrow) by virtue of a "hot spot" at the lower pole of the thyroid. The white contour indicates the position of the thyroid, the activity of which has been subtracted. Outside the thyroid, vascular activity is also seen (arrow heads). (b) At operation, an adenoma may be found arising from the lower parathyroid gland at its usual anatomical location (arrow). (c) An adenoma may also be found arising from an upper parathyroid gland which prolapses caudally to the lower pole of the thyroid and is suspended by a vascular pedicle (arrow).



(b) (c)

patients whose scans suggested a lower adenoma had an ipsilateral upper gland tumour at operation. In two of these cases, the adenoma was large (weighing 13200 and 2400 mg) and extended to the lower poles of the thyroid. Of the remaining six patients, it has been suggested that the vascular pedicle by which an upper gland is often suspended (Wang, 1975) allows a certain downward movement when the gland is enlarged. This vascular pedicle was positively identified and recorded in the operation notes in four out of these six patients. The downward migration may also be facilitated by a higher mobility of the upper parathyroid, as it is usually embedded in loose fatty tissue and may glide caudally under the thyroid capsule or beside the oesophagus (Akerstrom et al, 1984). This would then give rise to mislabelling the adenoma as arising from a lower gland (Fig. 1).

Correct pre-operative localization of an adenoma may help operative identification of the tumour and reduce the operating time (Hauty et al, 1987). Correct labelling of the origin of an adenoma is crucial in operative documentation. This is particularly true in cases where re-exploration is likely for recurrent hyperparathyroidism. A previously mislabelled excision may lead the surgeon to explore the wrong area, with a consequent increase in operating time and possible hazards. When unilateral neck exploration is advocated as the initial operation for primary hyperparathyroidism (Tibblin et al, 1982), mislabelling is most likely to occur, as the surgeon must then rely totally on the scintigraphic prediction of the anatomical location with no knowledge of the origin of the adenoma.

In conclusion, technetium–thallium subtraction scanning is a sensitive means of localizing parathyroid adenomas, correctly identifying the physical *location* of the adenoma. However, the *origin* of the tumour can only be determined at operation. An adenoma arising from the upper gland is likely to be mis-interpreted as a lower gland on the scan, because the upper gland has an inherently higher mobility and therefore a tendency to prolapse inferiorly to the lower pole of the thyroid when pathologically enlarged. Correct labelling of the adenoma by virtue of its origin is important, especially where re-exploration is likely for recurrent hyperparathyroidism.

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Complications in percutaneous transluminal angioplasty: relationships with patient age

By M. H. Morse, MRCP, FRCR, FDSRCPS, W. D. Jeans, FRCR, *S. E. A. Cole, BSc, D. Grier MRCP and D. Ndlovu, FRCR

Department of Radiodiagnosis and *Vascular Studies Unit, British Royal Infirmary, Bristol BS2 8HW, UK

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Keywords: Angioplasty, Complications

Abstract. Five hundred consecutive attempted lower limb angioplasties for ischaemic disease (370 patients, mean age 65.6 years, range 33–91 years) were reviewed. Significant complications occurred in 44 cases (8.8%). Nine patients (1.8%) underwent emergency surgery related to a complication. A further 12 patients (2.4%) underwent elective surgery related to a complication. In addition, four patients died within 30 days of the procedure; one following surgery performed because of a complication of angioplasty, one following a myocardial infarction, one following severe bleeding associated with subsequent thrombolytic therapy and one during emergency surgery related to a complication of angioplasty. A correlation was found between complication rate and age. This relationship was independent of the approach to, the position of, and the severity of the treated lesion. Elderly patients are at increased risk of complication in lower limb angioplasty.

The place of percutaneous transluminal angioplasty (PTA) in peripheral vascular disease is clearly established. Complications of PTA are well recognized, and in individual studies may be accurately assessed. Many authors have commented on the difficulty of comparison between such studies, as the results reflect not only differing populations and operator experience, but may also involve the use of differing reporting criteria. There have, however, been a number of recent major articles seeking to overcome these problems. In a review of 4662 non-coronary procedures (Becker et al, 1989), the overall incidence of complications was 10.2% but included complications of PTA at numerous sites in both the arterial and the venous circulation, so comparison with those studies which confine their results to the arterial system of the lower limb may not be entirely valid. Other reviews, concerned only with ilio-femoral-popliteal PTA, and in which the patient populations overlapped, showed complication rates of 11.4%, 3204 patients (Casarella, 1986), and 8.6%, 2043 procedures (Weibuhl et al, 1987). Complication rates in individual studies scrutinized for the latter review varied between 2% and 25%. Our experience suggested that elderly patients undergoing PTA in this department were experiencing a higher complication rate than younger patients, even when making some allowance for severity of disease. A formal relationship between complication rate and age has not been described in the literature, although it must be accepted that the small size of many of the published series may not allow the recognition of such statistical trends. We therefore reviewed the first 500 lower limb PTAs attempted in this department, in order to confirm or refute the presence of such a relationship.

Method

Five hundred lower limb PTAs were attempted at the Bristol Royal Infirmary in the period from October 1980 to July 1987. Multiple stenoses in the same anatomical vessel segment, or occlusions involving more than one segment were both classified as a single procedure; multiple stenoses in separate segments were classified according to the number of anatomical segments treated. Clinical indications included gangrene, rest pain, or intermittent claudication confirmed by a drop in ankle systolic pressure on exercise. Prior to PTA, ankle or brachial pressure indices were determined, and were reviewed 24 hours after PTA, and thereafter at set intervals throughout the follow-up period. Each PTA was performed by, or under the direct supervision of, a consultant or experienced senior registrar. One patient had ilio-femoral PTA performed via the axillary artery; all others had antegrade or retrograde aproaches from the femoral route. Gruntzig-type balloon dilatation catheters (Meditech, Boston USA) were used. Vasodilators were used in pressure gradient measurement, but not therapeutically except in the presence of recognized vascular spasm. Heparin (3000 units as a bolus intra-arterial dose) was administered immediately prior to dilatation of superficial femoral, profunda or popliteal lesions. Heparin was continued by infusion only in cases judged to be at particularly high risk of thrombosis (diffuse long segment disease, poor run off, or immobility). Each procedure was reviewed, within 1 week, at a combined meeting of members of the Departments of Radiodiagnosis, Vascular Surgery and the vascular Studies Unit. Senior members of each department were unchanged throughout the study period. Each procedure was assigned a case number, with a corresponding data sheet, in which clinical, haemodynamic,

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Address correspondence to Dr Morse, Department of Radiology, Frenchay Hospital, Frenchay, Bristol BS16 1LE.
Present addresses: Professor Jeans, Department of Radiology, Sultan Qaboos University, PO Box 32485 Al-Khod, Muscat, Sultanate of Oman and Dr Ndlovu, Department of Radiology, Godfrey Huggins Medical School, Avondale, Harare, Zimbabwe.

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and other factors, including complications, were recorded. Data were entered at presentation, at radiological diagnosis, at radiological or surgical intervention, and at follow-up. The study data were abstracted from these sheets. Complications were defined as follows.

1. *Dissections* were defined as those intimal tears caused by passage of guide wire or catheter prior to dilatation, which caused the procedure to be prolonged, modified (*e.g.* retrograde approach to an iliac lesion following failed contralateral cross-over approach) or abandoned. Dissections causing occlusion of a previously stenosed but patent vessel segment were not included in this section, and post-dilatation longitudinal tears were not recorded.
2. *Acute occlusion* was defined as luminal blockage in a previously stenosed but patent vessel segment shown during the initial angiographic procedure.
3. *Early occlusion* was defined as a fall in ankle blood pressure, with clinical signs and angiographic confirmation of thrombus occluding a vessel over a greater distance than the dilated segment, occurring after the patient had left the angiography suite, but within 24 hours of a technically successful dilatation.
4. *Peripheral embolization* was defined as clinically suggestive or angiographically proven embolization at a site distal to the dilatation.
5. *Haemorrhage* or *haematoma formation* was defined as significant only if sufficient to cause the procedure to be abandoned at any stage, or to require transfusion or surgical intervention.

The severity of stenoses and occlusions were retrospectively calculated using a combined stenosis/occlusion score, in which stenoses were scored conventionally, as an estimate of the percentage cross-sectional area of the lumen compromised, while occlusions were scored as 100 if less than 5 cm in length, 125 if 5–10 cm in length and 150 if greater than 10 cm in length.

Results were analysed using χ^2 tests, with Yates' correction for the smaller samples. Where numbers were so small that χ^2 techniques might be unreliable, exact probability tests were also applied. Standard error of mean assessments were applied to stenosis/occlusion scoring.

Results

Five hundred procedures were attempted in 370 patients, with a primary success rate of 85%. The mean age was 65.6 years (range 33–91); 75% were male. Age and sex distribution are shown in Fig. 1.

Complication occurrence is summarized in Tables I and II. Anatomical sites of treated lesions are shown in Table III.

There was a high complication rate during the first year of the study (16.6%), presumed to be because of operator inexperience. This rate rapidly fell, and remained relatively stable throughout the remainder of the study.

Complications occurred in 44 cases (8.8%). The majority (22; 4.4%) were non-occlusive dissections. In eight cases (1.6%) there was acute luminal occlusion, either due to dissection, or an indeterminate underlying mechanism. There were five instances (1%) where an initially uncomplicated procedure was followed by thrombosis in the dilated segment within 24 hours, four of which were successfully treated with streptokinase. Six episodes (1.2%) of clinically or radiographically apparent peripheral emboli were seen; one case required embolectomy, the others settled with conservative management. There were three episodes (0.6%) of puncture site haemorrhage sufficient to curtail the procedure; in each case a PTA had been performed, but treatment of a second more distal lesion was deferred. All episodes initially responded to conservative management, but one patient later developed a false aneurysm. There were no instances of vessel rupture or of dilatation balloons requiring surgical removal.

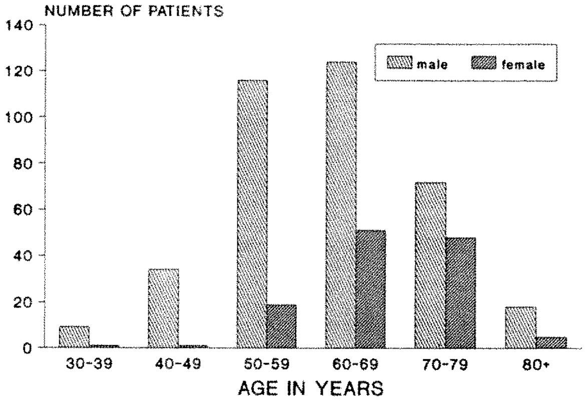

Figure 1. Age and sex distribution (all procedures).

Nine patients (1.8%) required emergency surgery for a complication of PTA. A further 12 patients (2.4%) underwent elective surgery related to complications.

Complication rates (Fig. 2), and the anatomical distribution of treated lesions both bore a strong relationship

Table I. Complications in each age group

Age	30–39	40–49	50–59	60–69	70–79	80+
Number in group	10	35	134	173	122	26
Complications	0	2	7	15	15	4

Table II. Total complications

Dissection (non-occlusive)	22
Acute occlusion	8
Early occlusion (thrombosis)	5
Peripheral emboli	6
Haemorrhage/haematoma	3
Total	44

Table III. PTA sites in each age group

Age	30–39	40–49	50–59	60–69	70–79	80+	Total
Iliac artery	7	24	68	99	38	6	242
Common femoral artery			1	3			4
Superficial femoral artery	2	9	55	58	65	17	206
Profunda femoral artery			1	3	2		6
Popliteal artery	1	2	10	9	17	3	42
Total	10	35	135	172	122	26	500

to age. The complication rate in patients over 70 years was significantly greater than that in patients below this age ($p < 0.02$, $\chi^2 = 5.82$, DF = 1). Stenosis/occlusion scoring (Fig. 3) showed a slight increase with increasing age, but this was not statistically significant.

There were four deaths within 30 days of the procedure, all in elderly patients.

Case 1

A man aged 81 years had successful dilatation of one iliac segment, but an occlusive dissection occurred when dilatation of the contralateral iliac was attempted. He was taken to theatre for an axillo-femoral graft, but following a stormy post-operative course, died 1 week later from broncho-pnemonia.

Case 2

A 73-year-old woman had an apparently successful popliteal dilatation, but with thrombosis of the same segment one day later. She was treated with an intra-arterial low dose thrombolytic infusion (10 000 units streptokinase and 250 units heparin per hour). An initial favourable response to thrombolysis was not maintained and, after 24 hours, the catheter was removed, haemostasis achieved, and the patient was systemically heparinized. Six hours after catheter withdrawal she became suddenly and profoundly shocked, dying within minutes in spite of resuscitative measures. Post-mortem revealed a massive haematoma tracking retroperitoneally from the puncture site.

Case 3

A 76-year-old man had a technically successful superficial femoral dilatation, but sustained a myocardial infarction within a few minutes of catheter withdrawal. He was resuscitated, but experienced a further, fatal infarct 4 days later.

Case 4

A woman aged 80 with extensive atheromatous disease had a dilatation of a common iliac stenosis performed via a contralateral cross-over approach. On withdrawl of the catheter she immediately complained of severe low abdominal pain, vomited and lost consciousness. Following resuscitation, her lower abdomen was cyanosed, and both legs were pulseless and white. She was taken immediately to theatre but became profoundly bradycardic and hypotensive during placement of an aorto-bifemoral graft, and did not regain consciousness. The aorto-iliac segment was found to be full of blood clot and ulcerated atheroma; the exact mechanism of injury could not be determined.

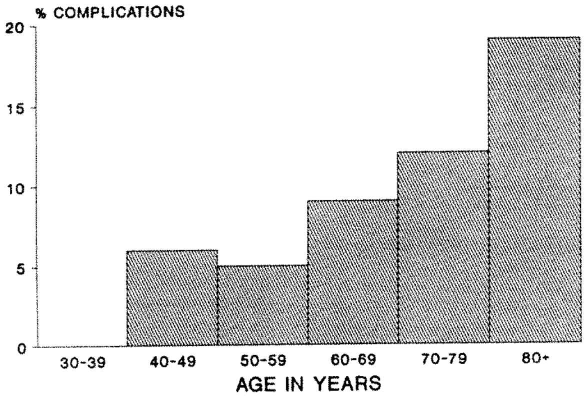

Figure 2. Complication rate by age group.

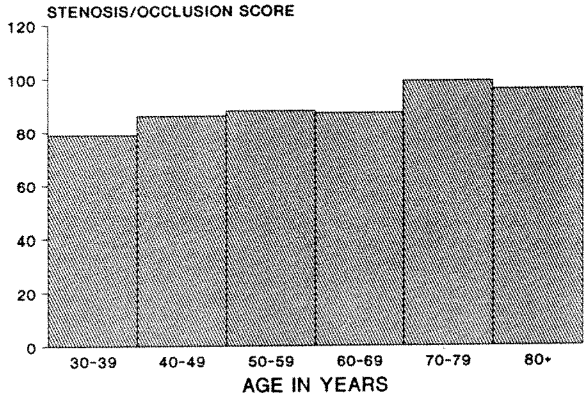

Figure 3. Distribution of stenosis/occlusion score by age group.

Discussion

The overall complication rate in this study (8.8%), and the relative contribution of specific complications to that total, is comparable to previous series (Casarella, 1986; Weibuhl et al, 1987; Becker et al, 1989).

The relatively high incidence of non-occlusive intimal dissection caused by initial passage of guide wire or catheter probably results from an aggressive reporting policy. This type of dissection is such a common occurrence during PTA that it is often regarded as a "radiological" rather than a "true" complication, and is therefore not included in many studies (Weibuhl et al, 1987). In the present study, non-occlusive dissection was recorded only if it caused the procedure to be prolonged or modified. None of the patients so recorded underwent surgery as a consequence of that complication. The removal of that sub-group, to allow direct comparison with studies which do not include a similar group, would result in a halving of the reported complication rate.

The presence of post-PTA intimal tears was not included in this study. Recently, this type of tear, particularly if extensive, has been seen as a possible indication for intra-luminal stent placement. Stenting procedures were not established during the study period, but critical assessment of such tears would now seem sensible.

There were eight episodes of acute occlusion of the dilated segment. In many instances it was not possible to be certain of the underlying mechanism involved; dissection, thrombosis and spasm have all been implicated in such cases (Gardiner et al, 1986).

Some authors have attempted to classify the degree of significance of complications by dividing them into major or minor groups (Weibuhl et al, 1987; Becker et al, 1989), but there seems to be general agreement that the most reliable guide to the importance of complications is the surgical intervention rate following PTA, particularly if this is recorded separately for complications, rather than for primary failures. Gardiner et al (1986), when reviewing the literature, quoted surgical intervention rates (*i.e.* urgent surgical treatment related to complications of PTA rather than to the underlying disease) ranging from 1% to 9%. The corresponding rate in this study was 1.8%, emphasizing the relatively benign nature of the majority of complications. Additionally, it is well recognized that many PTA complications do not need active treatment, and that even radiologically appalling complications may resolve with entirely conservative management (Gardiner et al, 1985). When complications are treated surgically, the procedure of choice is almost always the same as would have been the case had PTA not been available (Samson et al, 1984). The consequent procedure may, however, be much less serious than that initially planned, *e.g.* embolectomy rather than by-pass (Gardiner et al, 1986). It has recently been shown that acute occlusion of the iliac segment during PTA, a hitherto almost imperative indication for urgent by-pass surgery, can at times be treated with local, embolectomy type procedures (Train et al, 1988). Surgical options are thus rarely compromised by a complication of PTA.

A high complication rate does not in itself discredit PTA, for it is necessary to bear in mind the appreciable complication rate of conventional surgery. Review of comparable groups of PTA and surgical by-pass patients in this hospital (Cole et al, 1987) showed not only that long term patency rates were similar in both groups, but that morbidity was considerably higher in the surgical group. In a large scale review, significant morbidity occurred in 11.4% of aorto-iliac, and 6.7% of femoral by-pass procedures (Doubilet & Abrams, 1984).

The mortality rate in this study (1%) was a little higher than in most series, reflecting the use of 30-day mortality figures, as generally used to report surgical mortality. The accepted surgical mortality for aorto-iliac and femoral by-pass surgery is in the order of 4% (Doubilet & Abrams, 1984), agreeing well with experience at this centre, where the equivalent rate for the last 587 such procedures was 4.4%. As may be expected, a relationship exists between age and mortality rate for vascular operations, the mortality rate following 4815 lower limb by-pass procedures being 2.6% in patients under the age of 75, whereas the rate for 752 patients over 75 was 8.8% in the same study (Plecha et al, 1985). In one case in the present study (Case 2) the cause of death was related to "radiological" treatment of a PTA complication, but in only one case (Case 4) does it seem likely that the underlying cause was directly related to the PTA, although, for the reasons given, it was not possible to determine the exact mechanism of the acute event. In view of the precipitation of events by catheter withdrawl, direct trauma from the catheter tip must be presumed the likely cause.

The major finding of this study has been the increasing incidence of PTA complications with age (Fig. 2), this being significantly greater for patients over 70 years than for younger patients ($p < 0.02$). This relationship does not appear to have been previously described. Indeed, it is unusual to find any comment about the age structure of affected populations, although in a smaller sample, there was no difference in age range or mean age between patients with or without complications (Weibuhl et al, 1987). The relatively small number of complications experienced by a typical angioplasty population, together with the shape of the age distribution curve of that population, do however suggest that mean age alone would not be a powerful discriminant between complication and non-complication groups. In the present study, there was no significant difference between mean age in the complication (68.2 years) and non-complication groups (65.4 years). It is only by application of more detailed analysis that age-related differences appear, and it may well be that, had such analyses been applied to earlier studies, such a relationship would already have been described.

Three potential causes of this relationship were considered: first, that the lesions for dilatation were being approached in a physically different way in the older patients; secondly, that such lesions might have a different distribution in older patients; thirdly, that the older patients simply had more severe disease than the younger patients.

The physical approach to the lesion is only of significance in terms of iliac and common femoral segment disease, where contralateral "cross-over" antegrade or ipsilateral retrograde approaches are possible. Antegrade approach to the iliac/common femoral segment was not significant as a cause of complication when compared with a retrograde approach.

The anatomical distribution of lesions (Table III) was related to age groupings, with significantly greater numbers of distal (*i.e.* superficial femoral, popliteal/profunda) than proximal (*i.e.* iliac/common femoral) lesions being treated in the older age groups. An apparent relationship thus exists between the distal lesions and complication rate, but this is, however, not in itself evidence of cause and effect, for that would require the distal lesions to be associated with a higher complication rate. There was no significant difference between the total numbers of proximal or distal lesions, or between the complication rates in those groups.

The use of a scoring system for stenoses and occlusions which provides a continuum across the range of atheromatous disease shows that there is a gradual increase in severity of treated disease with age, but that this is not statistically significant. There were also no significant differences between the stenosis/occlusion score with regard to proximal or distal lesions, or between the scores in the complication or non-complication groups.

We conclude that, in PTA, a relationship exists between age and complication rate, and that this relationship is independent of the approach to the lesion, the position of the lesion, and the severity of the lesion. Increasing age is therefore, in itself, a risk factor for complication in PTA. This finding may modify attitudes towards intervention in the elderly.

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Magnetic resonance angiography of abdominal vessels: early experience using the three-dimensional phase-contrast technique

By P. Vock, MD, F. Terrier, MD, H. Wegmüller, MD, *F. Mahler, MD, †Ph. Gertsch, MD, §S. P. Souza, PhD and §C. L. Dumoulin, PhD

Departments of Radiology, *Internal Medicine, and †Visceral Surgery, University of Berne, Switzerland and §Research and Development Center, General Electric Company, Schenectady, New York, USA

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Abstract. Based on three-dimensional acquisition of three sequences sensitive to one flow-direction, abdominal magnetic resonance phase-contrast angiography (MRA) was performed in 13 volunteers and 20 patients. The subjects received no antiperistaltic medication and were allowed to breath normally during the three acquisition periods of 11 minutes. The frequency of demonstration of the normal aorta, superior mesenteric and right and left renal arteries was 100%/100%/91%/100%, and of the inferior vena cava, splenic, superior mesenteric and portal veins was 92%/67%/92%/100%, respectively, whereas other abdominal vessels were seen less constantly. In renal artery stenosis or occlusion, MRA detected eight out of nine pathological arteries, missed only a minimal stenosis and was never false positive. In all 10 cases of portal hypertension, MRA demonstrated the venous collaterals detected by conventional angiography and in six cases showed more collaterals, particularly paravertebral vessels. A Budd–Chiari syndrome was investigated as well. If the accuracy of MRA can be proved in larger studies, it may become an important diagnostic tool in evaluating abdominal vascular pathology, such as renal artery stenosis or portal hypertension.

Radiological angiographic methods, although they give excellent morphological information, involve ionizing radiation, the risk of side reactions to contrast media and a varying degree of invasiveness. Duplex sonography can overcome some of these disadvantages, but the access to deeper vessels may be difficult or impossible in the abdomen. Magnetic resonance angiographic methods have been introduced recently and afford functional flow information rather than morphological imaging (Wedeen et al, 1985a, 1985b; Dumoulin & Hart, 1986; Alfidi et al, 1987; Dumoulin et al, 1988, 1989a; Laub & Kaiser, 1988). Most applications have focused on the head, neck and extremities, whereas the trunk of the body with its physiological motion was initially neglected because of difficulty with breathing and peristalsis artefacts.

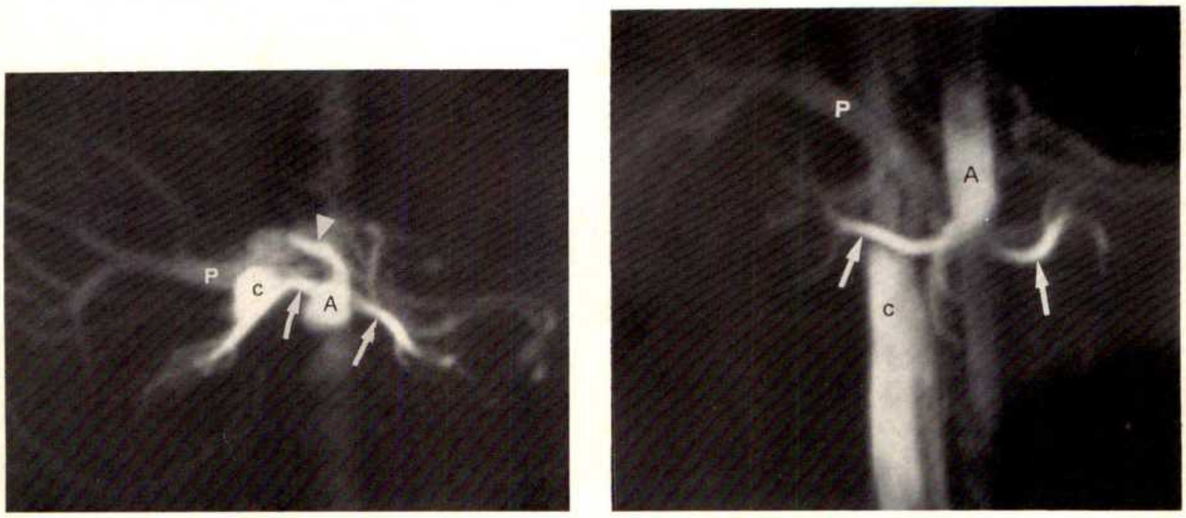
This article reflects our 8-month experience with phase-contrast MR angiography (MRA) using three-dimensional acquisition (Dumoulin et al, 1989a). The purpose of the study was to test the detectability of normal abdominal vessels and to assess the potential applications of MRA to vascular disease, especially renal artery stenosis and portal hypertension.

Methods

A 1.5 tesla imaging system with a shielded gradient coil subsystem (Signa, General Electric Co., Milwaukee, USA) was used. Flow-sensitive images were generated by a fast-imaging three-dimensional phase contrast technique (Dumoulin et al, 1989a). The field of view was 40 cm in the axial plane (256 left–right frequency encoding steps and 128 anteroposterior phase encoding steps) and 20 cm in the superoinferior dimension (128 phase encoding steps), occasionally 10 cm (for a matrix of 64). With a time to repeat (TR) of 20 ms, an echo time (TE) of 10 ms, a flip angle of 20° (occasionally 10°) and two excitations, one volume-study lasted roughly 11 minutes (5.5 minutes respectively for the matrix of 64). Three such acquisitions were obtained to encode flow in all three directions. The three-way modulus method (square root of the sum of the squares) was used to combine all 128 (64) triplets pixel by pixel into 128 (64) axial images, each containing three-dimensional flow information. By the maximum pixel method, images of all axial anatomical planes were then both collapsed into one axial image (Fig. 1a) and projected into 32 coronal and oblique planes at view angle steps of 3.2° (Fig. 1b). These were analysed three-dimensionally using a video loop.

The same safety instructions and checks were taken as for ordinary MRI. However, using a research software, we did not control the specific absorption rate (SAR). Informed consent was given. The patients were all studied in the supine position, their abdomen being mildly compressed with a wide strap attached to the table. No medication was used to reduce gastrointestinal peristalsis, and the subjects were allowed to breath normally during the entire acquisition period.

Thirteen normal volunteers (five female, eight male; aged 8–43 years) were studied. Ten had the ordinary protocol. In two we used a saturation pulse placed superiorly to the imaging volume in order to suppress the signals from the protons in the heart and the aorta; therefore, we were not able to analyse the arteries. In one volunteer the field of view was centred lower to include only the level of the renal vessels. A vessel was



(a) (b)

Figure 1. Normal three-dimensional phase-contrast MRA of the abdomen. (a) Axial view of 128 slices collapsed using the maximum intensity method. (b) Anteroposterior projection of the same data presented in (a). A: aorta; C: inferior vena cava; short arrows: renal arteries; arrow head: superior mesenteric artery; P: portal vein. Note the decrease of flow signal in the infrarenal aorta and, less obviously, in the suprarenal inferior vena cava.

considered to be detectable when its main portion was seen without an interruption of more than 5 mm.

Twenty patients (11 female, nine male; aged 21–84 years) were studied by MRA for the presence of pathological vessels and the absence of normal vessel signals without knowledge of the results of other investigations. Nine were suspected of having renal artery stenosis or occlusion. Following the MRA study, all had conventional catheter angiography. Three had normal renal arteries, three unilateral stenosis or occlusion and three bilateral stenosis (nine pathological renal arteries). Three patients with four diseased arteries were also studied by MRA after percutaneous transluminal angioplasty (PTA).

The other 11 patients had portohepatic disease; all were studied by duplex sonography, nine by catheter angiography, eight by dynamic computed tomography (CT) and seven by magnetic resonance imaging (MRI). Ten patients had portal hypertension, three from extrahepatic and seven from intrahepatic portal venous obstruction; eight had cirrhosis, two hepatocellular carcinoma and one cholangiocarcinoma. One patient also had the Budd–Chiari syndrome caused by a malignant tumour.

Results

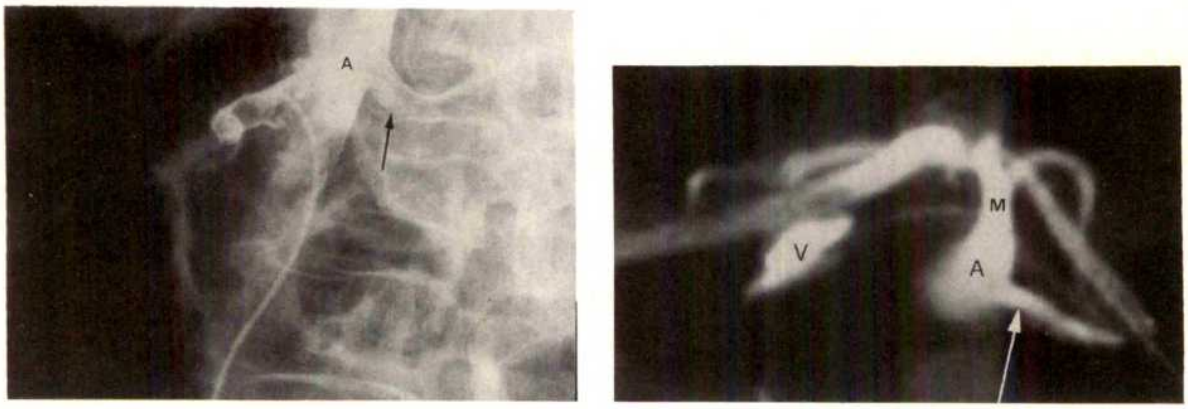
Using the standard protocol without spatial saturation, the suprarenal aorta, superior mesenteric and left renal arteries were always and the right renal artery nearly always detected in volunteers (Fig 1; Table I). However, in the infrarenal aorta flow signal was always weaker than suprarenally and in three cases nearly absent. At the point of maximal inferior convexity of the renal arteries there was a short interruption of less

Table I. Abdominal MRA in normal volunteers: vessel detectability ($n = 13^a$)

Arteries		Veins	
Aorta: suprarenal	11/11 (100%)	Vena cava	12/13 (92%)[b]
infrarenal	8/11 (73%)	Hepatic: right	7/12 (58%)
		middle	7/12 (58%)
Common hepatic	2/10 (20%)	left	0/12 (0%)
		Portal	10/12 (83%)
Splenic	6/10 (60%)	Splenic	8/12 (67%)
Superior mesenteric	10/10 (100%)	Superior mesenteric	11/12 (92%)
Renal: right	10/11 (91%)	Renal: right	6/13 (46%)
left	11/11 (100%)	left	8/13 (62%)

[a] In two studies, saturation of inflowing aortic flow was used, so that analysis of arteries was not possible; one study was limited to the renal vessels.

[b] In four out of the 12 the signal intensity was much higher in the infrarenal than in the suprarenal vena cava.



(a) (b)

Figure 2. Embolic occlusion of the right renal artery documented by conventional angiography (a) and by MRA (b); the axial view demonstrates normal flow in the left renal (arrow) and superior mesenteric artery (M), but no flow signal in the right renal artery. A: aorta; V: inferior vena cava.

than 5 mm of the renal artery signal in most of these normal volunteers. A good, nearly continuous signal from the splenic artery was observed in six of 10 volunteers, but only in two from the common hepatic artery. The inferior vena cava, left and right renal veins were well visualized in 92%, 62% and 46%, and the splenic, superior mesenteric and portal veins in 67%, 92% and 83%, respectively. Although visible, vena caval flow was often considerably weaker in the suprarenal than the infrarenal segment. The right and middle hepatic veins were shown in 58%, whereas the left hepatic vein was never more than segmentally demonstrated.

In suspected renal artery pathology, MRA was truly negative in the three subjects with normal renal arteries. It correctly demonstrated reduced or absent signal over a long distance of more than 5 mm in eight out of nine renal artery stenoses or occlusions (Figs 2 and 3; Table II), and showed normal signal intensity in one artery with minimal stenosis by conventional angiography which was not treated by PTA. In all four arteries of the three patients with a follow-up study, the signal intensity of the stenosed artery was slightly increased 1 day after PTA (Fig. 3c).

Table III compares the results of MRA ($n=10$) and of catheter angiography ($n=8$) in portal hypertension. Well-known collateral pathways (coronary, umbilical, short gastric and periportal veins) could be demonstrated by both methods, and MRA was at least as sensitive as catheter angiography (Fig. 4). It additionally showed curled paravertebral veins in eight out of 10 patients not seen with conventional angiography in the same patients. In one case with a history of bleeding due to portal hypertension, MRA, conventional angiography and duplex sonography were all unable to demonstrate collaterals. In one patient with neoplastic Budd–Chiari syndrome (Fig. 5), MRA demonstrated a high-grade stenosis of the right and middle hepatic veins and even more venous collaterals than detected by MRI, angiography and sonography.

The following were also detected: a supernumerary renal artery in one volunteer and two patients, a right hepatic artery arising from the superior mesenteric artery in a patient and a left ovarian vein in a volunteer.

Discussion

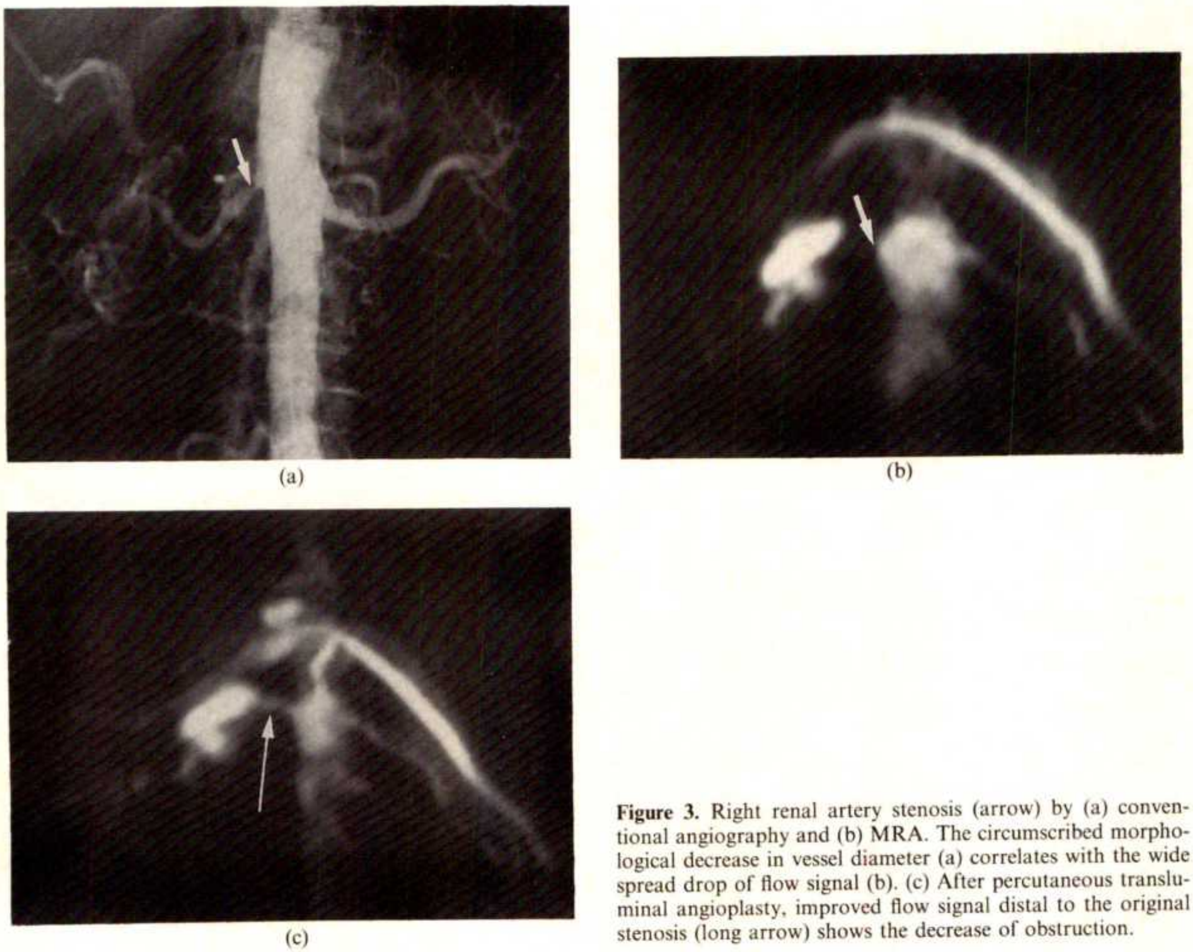
Vascular disease has become one of the most common medical problems. Although there are several vascular imaging methods, each has its limitations. Conventional X-ray angiography is invasive, involves ionizing radiation and the risk of iodized contrast agents, and generally demonstrates only the injected territory. Duplex ultrasound avoids these disadvantages and offers quantitative flow information; however, its field of view is often limited and access to specific deep vessels may be difficult or impossible. Other tomographic methods, like CT and MRI, in addition to sharing some of these limitations, do not afford a topographic overview and the spatial resolution needed for small vessels. Despite its cost, a non-invasive imaging method with three-dimensional presentation capabilities like MRA might add to the spectrum of diagnostic methods.

Table II. MRA of renal arteries with conventional angiographic correlation

Conventional angiography	Number of patients[a]	MRA signal intensity		
		Normal	Reduced	Absent
Normal artery	9	9	0	0
Embolic occlusion	1	0	0	1
Stenosis	8	1[b]	3	4

[a] Number of patients: 9; number of arteries: 18.

[b] Minimal degree of stenosis in fibromuscular hyperplasia at conventional angiography that did not justify percutaneous transluminal angioplasty.



(a)

(b)

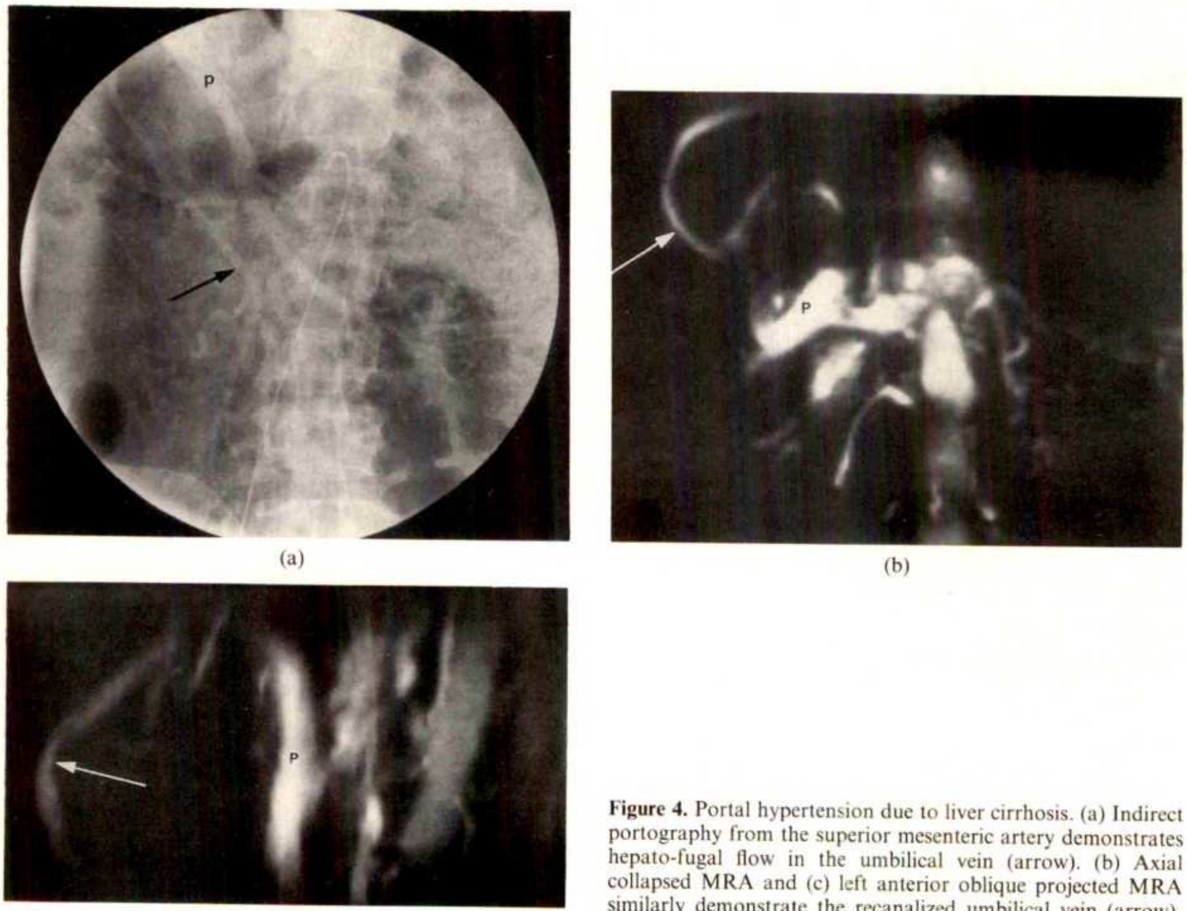
(c)

Figure 3. Right renal artery stenosis (arrow) by (a) conventional angiography and (b) MRA. The circumscribed morphological decrease in vessel diameter (a) correlates with the wide spread drop of flow signal (b). (c) After percutaneous transluminal angioplasty, improved flow signal distal to the original stenosis (long arrow) shows the decrease of obstruction.

Table III. MRA in portal hypertension: detectability of collaterals

Patient	Collaterals						
	Periportal	Coronary	Paraumbilical	Short gastric	Retroperitoneal (splenorenal)	Paravertebral	Other
R.O.	−/−	+/+	+/−	+/+	−/−	+/−	−
R.E.	−/−	+/−	+/+	−/−	−/−	+/−	Epigastric +/−
E.B.	−/−	+/+	+/+	−/−	−/−	+/−	−
S.T.	−/−	−/−	−/−	+/+	−/−	+/−	−
M.U.	−/−	−/−	−/−	−/−	−/−	−/−	Left ovarian +/+
S.A.	+/+	−/−	−/−	−/−	+/−	+/−	−
S.C.	+/−	−/−	+/−	−/−	−/−	+/−	−
F.R.	−/−	−/−	−/−	−/−	−/−	−/−	−
F.U.	+/0	−/0	+/0	+/0	+/0	+/0	−
B.O.	−/0	−/0	+/0	−/0	−/0	+/0	−
MRA ($n=10$)	3	3	6	3	2	8	2
Conventional X-ray angiography ($n=8$)	1	2	2	2	0	0	0

The first + (visualized), − (not visualized) or 0 (not performed) gives the result of MRA; the second gives that of conventional angiography.



(a)

(b)

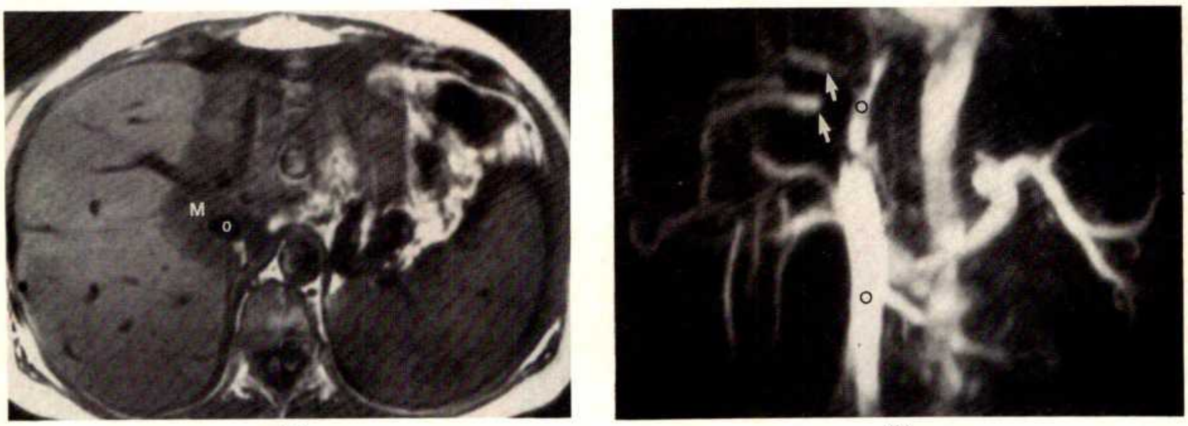
(c)

Figure 4. Portal hypertension due to liver cirrhosis. (a) Indirect portography from the superior mesenteric artery demonstrates hepato-fugal flow in the umbilical vein (arrow). (b) Axial collapsed MRA and (c) left anterior oblique projected MRA similarly demonstrate the recanalized umbilical vein (arrow). Portal vein: P.

Magnetic resonance angiography is based on the two prerequisites of sensitizing the signal to flow and of suppressing signal from static tissue. Two principal solutions have been realized, time-of-flight (Laub & Kaiser, 1988; Dumoulin et al, 1989b, Edelman et al, 1989a; Keller et al, 1989) and phase-sensitive techniques (Weeden et al, 1985a, 1985b; Dumoulin & Hart, 1986; Dumoulin et al, 1989a). Time-of-flight MRA depends on flow-related enhancement using either wash-in or wash-out phenomena, whereas phase-contrast MRA relies on flow-dependent phase shifts and a subtraction technique to detect flow in the readout, the phase-encoding or the projection direction. Volumetric acquisition (three-dimensional Fourier-transformation) (Dumoulin et al, 1989a, 1989b) affords smaller voxels with less signal loss due to magnetic susceptibility effects than sequential acquisition of two-dimensional sections. We used this with the phase-contrast technique and had to accept a longer acquisition time. Thus, in contrast to the two-dimensional time-of-flight and phase contrast methods we could not avoid respiratory motion by measuring during apnea. In a recent article, Edelman et al declared breath-holding a prerequisite for high-quality angiograms of body regions subject to motion artefact (Edelman et al, 1989a). Our results both in normals and in patients prove it is possible to demonstrate most major abdominal vessels during normal respiration and without antiperistaltic medication. The superior mesenteric and both renal arteries as well as the portal vein and its tributaries are reliably seen in a high percentage. Physiological abdominal aortic flow at rest above all maintains renal and visceral perfusion and, thus, is less in the infrarenal segment. On the other hand, the signal drop within the suprarenal vena cava seen in normal volunteers is most likely caused by flow pulsatility, as known from Doppler studies.

Certainly, artefacts are common, such as those arising from the heart and the aorta in the phase-encoding direction that destroy the signal from the left hepatic vein. Our results still need to be improved if MRA is to contribute useful information on other abdominal vessels. However, we are confident that this will be possible with ongoing hardware and software adaptation and with new methods of saturation and motion compensation. Another new development is quantification of flow, and initial experience is very promising (Edelman et al, 1989b; Maier et al, 1989).

Already, MRA is useful in difficult clinical cases, for



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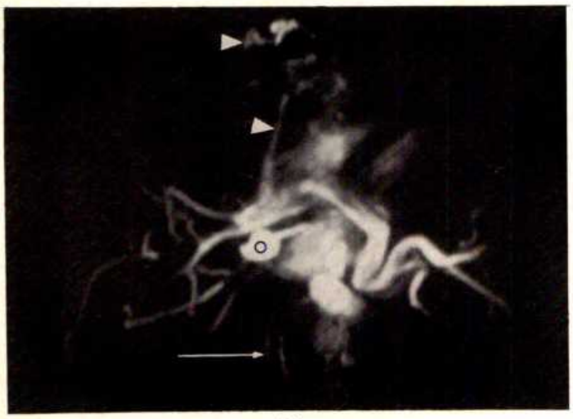

(c)

Figure 5. Budd–Chiari syndrome and portal hypertension due to cholangiocarcinoma. (a) Axial MRI demonstrates the hypointense central mass lesion (m) infiltrating around the inferior vena cava (o) and splenomegaly. (b) Anteroposterior projection MRA confirms the functional stenosis of both the right and middle hepatic veins (arrows) and the inferior vena cava (o). (c) Portal hypertension is better demonstrated on the axial view by collaterals both of the umbilical/anterior abdominal veins (arrow heads) and the paravertebral veins (long arrow).

instance when iodized contrast agents or invasive angiography are contra-indicated. If our results can be confirmed in larger series, MRA might be used as a screening method for significant renal artery stenosis. We obtained a sensitivity of 89% and missed only one probably not significant stenosis. The fundamental difference between morphology-oriented conventional angiography and functional MRA must be emphasized. For instance, with significant stenosis in the order of 50% to 90%, MRA showed a complete signal void in the entire extrarenal segment of the renal artery beyond the point of obstruction. Likewise, the obviously physiological circumscribed signal drop at the point of inferior convexity of renal arteries correlated with normal morphology and might be caused either by dephasing due to intravoxel velocity gradients or by higher order motion. If this is true, loss of signal will be minimized with shorter TE. Currently, we do not know whether the morphological information of conventional angiography or, despite decreased spatial resolution, the functional information of MRA will give a better differentiation of significant stenosis. Furthermore, in residual or recurrent arterial hypertension, a non-invasive test for follow-up studies after PTA of renal artery stenosis would be extremely welcome. It is certainly too early to judge the value of MRA in detecting stenosed supernumerary renal arteries.

Magnetic resonance phase-contrast angiography may soon have a significant role in portal hypertension. Although our phase-contrast method currently does not quantify flow, we add to the recent communication of four patients using the time-of-flight technique (Edelman et al, 1989c) with our angiographically correlated data on 10 patients. In our experience MRA was at least as sensitive as and several times better than conventional angiography in demonstrating portosystemic and portohepatic collaterals. Specifically, we observed pathological paravertebral vessels not demonstrated by other methods. These probably represent portosystemic retroperitoneal collaterals and are not shown well angiographically on usual projections. Since any method using local contrast injection will reach only part of the portal territory, indirect arterial portography, splenoportography and transhepatic portography have special limitations as well as their invasiveness. However, MRA is sensitive to any laminar flow within the entire field of view without contrast injection and the potential risk of iodized contrast agents. Since the signal of MRA is based on flow, watershed collaterals with minimum flow may theoretically escape detection by this method. The non-invasive combination of spatially limited quantitative duplex sonography with the global survey of MRA may overcome such problems.

Our protocol may be used to investigate veins other than the portal system, as illustrated by the case of Budd–Chiari syndrome. It will have to be adapted to any specific problem, *e.g.* switching the readout and the phase-encoding directions and using spatial arterial saturation might allow demonstration of all three hepatic veins.

In conclusion, MRA of abdominal vessels is still in the phase of clinical development. Because its quality is not significantly degraded by respiration, the three-dimensional phase-contrast method is an alternative to the two-dimensional time-of-flight technique with multiple sections during apnea. Renal artery stenosis and portal hypertension are currently the promising areas of application. Depending on confirmation of results by larger series, MRA might be used for screening or, combined with duplex sonography, occasionally replace conventional angiography.

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Ultrasound in the investigation of the right iliac fossa mass

By F. C. Millard, FRCS, M. C. Collins, FRCR and R. J. Peck, FRCR

Department of Radiology, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF

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Keywords: Ultrasound, Right iliac fossa, Mass

Abstract. Patients presenting with a right iliac fossa (RIF) mass are a diagnostic problem. The objective of this study was to assess the role of ultrasound (US) in their investigation. A prospective series of 50 patients presenting with a clinically suspected RIF mass was examined by US and the findings correlated with the final diagnosis. There was a positive finding in 34 patients (68%). Ultrasound correctly identified the organ of origin in 33 (97%) and was able to guide the patients' further management. In 12 cases no abnormality was found in the RIF, of which 11 had no positive findings at follow-up and one was shown to have an unrelated abnormality at laparotomy. In four cases the findings were due to normal variants. Ultrasound is the imaging modality of first choice in patients presenting with a RIF mass.

Patients presenting with a right iliac fossa (RIF) mass are a clinical diagnostic puzzle. Frequently, these patients have a series of investigations including barium enema and intravenous urography, which are often inconclusive.

When an RIF mass is palpable it should be demonstrable by ultrasound (US) and therefore it should be possible to assess its organ of origin, and give some idea of its nature. Conversely, a normal US may exclude a lesion and prevent further unnecessary imaging, particularly if involving ionizing radiation.

It was decided to perform a prospective study to assess the role of US in the investigation of these patients, and to determine any US features of RIF masses which may help establish their nature.

Method

A prospective study of 50 consecutive patients, presenting with the clinical diagnosis of an RIF mass and referred for US at the Royal Hallamshire Hospital, was carried out between January and August 1989. Their ages ranged from 18 to 94 years (mean 61 years). Thirty-six were female and 14 male.

The US was performed by a consultant radiologist using an ATL Ultramark 4 scanner with 3 MHz and 5 MHz sector transducers. A full abdominal scan was also performed routinely.

The findings were confirmed by further imaging, laparotomy or in a few cases clinical follow-up.

Results

Thirty-four patients (68%) were shown to have a lesion corresponding to the palpable RIF mass. In four patients the mass was due to a normal variant (two—low lying kidney, two—Riedel's lobe), and in 12 no mass was visualized in the RIF.

Of the 34 masses, US correctly identified the organ of

Table I. Findings in patients with gastro-intestinal pathology

Clinical diagnosis	US diagnosis	Final diagnosis	Method
Ca. caecum	Appendix mass	Ca. caecum	Laparotomy
Ca. caecum	Ca. caecum	Ca. caecum	Laparotomy
Ca. caecum	Ca. caecum	Ca. caecum	Laparotomy
Cholecystitis	Ca. caecum, hepatic mets.	Ca. caecum, hepatic mets.	Laparotomy
Ca. caecum	Ca. caecum	Ca. caecum	Laparotomy
Ca. caecum	Ca. caecum	Ca. asc. colon	Laparotomy
Ca. caecum	Ca. caecum	Ca. caecum	Laparotomy
Ascites	Ca. colon	Ca. caecum	Laparotomy
Retroperitoneal mass	Crohn's disease	Ca. caecum	Laparotomy
Ca. caecum	Ca. caecum	Ca. caecum	Laparotomy
Ca. colon	Abnormal signoid ? cause	Ca. sigmoid	Laparotomy
Ca. colon recurrence	Ca. colon		Clinical
Ca. colon	Ca. caecum	Lymphoma caecum	Laparotomy
Appendix mass	Ca. caecum	Appendix mass	Laparotomy
Ca. caecum	Ca. caecum	Appendix mass	Laparotomy
Appendix mass	Inflammatory mass	Appendicitis	Laparotomy
Crohn's disease	Crohn's disease	Crohn's disease	Small bowel enema
Crohn's disease	Crohn's disease	Crohn's disease	Laparotomy

Table II. Findings in patients with genito-urinary tract pathology

Clinical diagnosis	US diagnosis	Final diagnosis	Method
Polycystic kidney	Polycystic kidney	Polycystic kidney	US (previous IVU)
Pelvic abscess	Ectopic pregnancy	Ectopic pregnancy	Laparotomy
Ovarian ca.	Ovarian ca.	Ovarian ca.	Laparotomy
Ca. caecum	Ovarian cyst	Ovarian cyst	Laparotomy
Mass ? cause	Ovarian cyst	Ovarian cyst	Laparotomy
Mass ? cause	Hypernephroma	Hypernephroma	Laparotomy
Pelvic abscess	Ovarian cyst		Clinical

origin in 33. Eighteen of these were gastro-intestinal and the pathology was correctly suggested in 14 (Table I). Seven masses were arising from the genito-urinary tract, and US was correct in all seven (Table II). In a further nine patients, the mass arose from another organ system, and US made the correct diagnosis in seven (Table III).

Of all the cases studied, the site of origin was wrongly suggested by US in only one. This was a 71-year-old female patient on anti-coagulant therapy, who presented with lower abdominal pain, constipation, and a tender RIF mass. Clinical assessment suggested a complicated ovarian cyst. Ultrasound showed a complex mixed-echo mass anterior to the bladder. The appearances were difficult to interpret, and bowel malignancy was suggested. At laparotomy, however, an extensive rectus sheath haematoma was found.

In the 12 patients in whom no mass was found at US, six underwent no further imaging. Of the remainder, five had a barium enema, of whom two also had a small bowel enema. No further pathology was demonstrated. One patient had the clinical picture of large bowel obstruction, and at laparotomy was found to have a carcinoma of the transverse colon and no actual mass in the RIF.

Of the four patients in whom US found an anatomically normal variant of kidney or liver, two had no further imaging and two had a barium enema.

As far as can be determined, therefore, of the 12 patients with "negative" US there were no false negatives (excluding the one patient who later was found to have a carcinoma of the transverse colon).

Discussion

In any patient with a palpable RIF mass, we felt US should be the primary investigation. This suggestion was also made in a recently published retrospective study of US in the palpable abdominal mass (Barker & Lindsell, 1990).

A normal US may exclude a lesion and prevent further unnecessary imaging. Our study confirmed this, US being highly specific (100%) in excluding the presence of an RIF mass (Table IV). Equally, our study found US to be highly sensitive (100%) in correctly identifying patients with an RIF mass (Table IV). We have found US to be highly accurate in identifying the organ of origin of the mass (97%) as compared with clinical assessment (76%).

Ultrasound has always been thought to be of limited value in evaluating bowel problems, but gradually it is being shown to have much value in this area (Gholkar & Khan, 1989). The US features of appendicitis (Puylaert, 1986; Jeffrey et al, 1988), Crohn's disease (Sonnenburg et al, 1983), and Campylobacter enteritis (Puylaert et al, 1988) have all recently been described. Some ultrasonologists feel that a general review of the abdomen during

Table III. Findings in patients with non-gastro-intestinal or non-genito-urinary pathology

Clinical diagnosis	US diagnosis	Final diagnosis	Method
Ca. caecum	Hepatomegaly, metastases	Hepatic mets.	Liver biopsy
Pancreatitis	RIF abscess, pancreatitis	Pancreatitis, abscess	Laparotomy
Intestinal obst. strangulated inguinal hernia	Small bowel obstruction, inflammatory mass hydrocoele	Obstruction, adhesions	Laparotomy
Carcinoid syndr.	Carcinoid tumour mass	Carcinoid mass	Laparotomy
Ca. caecum	Aortic aneurysm	Aortic aneurysm	CT
Appendix mass	Ca. caecum	Rectus sheath haematoma	Laparotomy
Pelvic abscess, post E.R.C.P.	Abscess	Retro-peritoneal abscess	Laparotomy
Wound abscess	Incisional defect	Stitch granuloma	CT
Ca. caecum	Ascites, thickened bowel	*	

*94-year-old woman. Patient died—no post-mortem.

Table IV. Sensitivity and specificity of US in assessing RIF mass

	Mass present	Mass absent	Total
Ultrasound positive	38	0	38
Ultrasound negative	0	12	12
Total	38	12	

an ultrasound examination can provide significant useful information, particularly in the detection of occult neoplasms (Price & Metreweli, 1988).

The correct pathological diagnosis was made by US in 82% of cases. Although we were able to determine bowel as the cause of the mass in all the 19 cases in which this proved so, it was more difficult to differentiate neoplastic from inflammatory lesions.

In conclusion, this prospective study found US, in experienced hands, to be accurate in assessing RIF masses, with the advantage that it is non-invasive and does not involve the use of ionizing radiation. It should be the first investigation of choice in these patients.

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Determinations of organ doses and effective dose equivalents from computed tomographic examination

By Kanae Nishizawa, PhD, *Takashi Maruyama, PhD, Makoto Takayama, MD, Minoru Okada, MD, Jun-ichi Hachiya, MD and Yoshiro Furuya, MD

Department of Radiology, School of Medicine, Kyorin University, 6–20–2, Shinkawa, Mitaka, Tokyo 181 Japan and *Division of Physics, National Institute of Radiological Sciences, 9–1, Anagawa-4-chome, Chiba 260, Japan

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Abstract. The organ or tissue doses were determined with a phantom measurement for 12 types of CT scanners widely used in Japan. Two types of thermoluminescent dosimeters were used for the dose determinations in a Rando woman phantom. The effective dose equivalents recommended by the International Commission on Radiological Protection were calculated using the measured organ or tissue doses. It was found that the CT scanners currently available give quite different organ or tissue doses. When selecting the optimum technical factors for scanning, therefore, it is important to take into consideration the balance of the image quality and the radiation exposure to patients.

Computed tomography (CT) has brought about the greatest improvement in diagnostic radiology since the discovery of X rays. The availability and usefulness of CT was quickly recognized and technical development has proceeded very rapidly. However, the introduction of CT scanners gave rise to a significant problem in the specification of radiation doses imparted to patients from CT examinations. The problem is the non-uniformity of dose distribution within the patient: in most practical CT examinations, a number of CT slices may be contiguous or overlapping.

The experimental determination of the dose distribution resulting from typical CT examinations with different types of CT scanners has been reported by several authors using standard dosimetry techniques (Shope et al, 1982; Murphy & Heaton, 1985; Hude & Sandison, 1985, 1986; McCrohan et al, 1987). We have previously determined organ or tissue doses during head and whole-body scannings with an EMI 5005-CT scanner, using a thermoluminescent dosimeter (TLD) and an average-woman Rando phantom (Nishizawa et al, 1979). We have also evaluated the population doses and radiation risks for genetic effects and carcinogenesis including leukemia, on the basis of a nationwide survey in Japan (Nishizawa et al, 1981a). At that time, eight different types of CT scanners were used for the evaluation of organ or tissue doses (Nishizawa et al, 1981b).

Recently, new types of CT scanners have become available in Japan. In this paper we report organ or tissue doses determined with a phantom measurement for 12 types of CT scanners widely used throughout Japan, in order to evaluate the population doses and radiation risks from recent CT examinations. The effective dose equivalents recommended by the International Commission on Radiological Protection (ICRP) were calculated using the resultant organ or tissue doses.

Methods

The CT scanners used for the present measurements were the 12 different types of machines listed in Table I. These are typical CT scanners frequently used for routine clinical examinations in Japan. The dose measurements were carried out in the radiographic rooms where the CT scanners were routinely operated. A Rando woman phantom produced by the Alderson Research Laboratory was used as a model Japanese patient. The woman phantom corresponds to a complete body, 163 cm high and 54 kg in weight, and consists of a total of 35 slices. The woman phantom was converted to an average-man phantom by removing its breasts.

Two types of TLD were used to determine experimentally the organ or tissue doses in the phantom: Panasonic UD-170A(BeO) TLDs were used in the measurement of useful X-ray beams and Panasonic UD-110S($CaSO_4$:Tm) TLDs for the determination of the lower level of radiation doses outside useful beams. The UD-170A TLD has an effective atomic number of 7.6 comparable to the tissue value of 7.4, and, therefore, is not suitable for low level dose measurements. The UD-110S TLD consists of a high atomic number phosphor (effective atomic number: 14.4) dosimeter with a much higher energy dependence than BeO, and is suitable for low level measurements. The 170A and 110S TLD were used as rods with dimensions 2 mm in diameter and 12 mm length. The TLDs were preselected to have a sensitivity within 7% of the mean value. Each batch of TLDs was calibrated prior to use.

Since the quality of X rays depends on the CT scanner, it is difficult to calibrate the TLDs for X rays from the CT scanner used in the measurement. Assuming that the X-ray quality is principally dependent on technical parameters such as tube voltage, tube

Table I. Characteristics of CT scanners

Scanner	A	B	C	D	E	F	G	H	I	J	K	L
	CT9000 Series II	CT Max II	CT Pace GX	CT9800Q	TCT60A 30	TCT60AX	TCT 600HQ	TCT 900S	TCT 300S	CT/W 600	SCT 2500T	SOMATOM DR Ver. G
Generation	3	3	3	3	3	3	3	New4	3	3	3	3
Targetmaterial	W	W	W	W	W-Mo	W-Mo	W-Mo	W-Mo	W-Mo	W	W	W
Focus size (mm × mm)	1.2 × 1.2	0.6 × 0.6	0.7 × 0.9	0.7 × 0.9	1.0 × 1.0	1.0 × 1.0 1.1 × 1.1	0.9 × 0.9	1.2 × 1.6 0.8 × 0.9	1.1 × 1.1	1.1 × 1.5 0.8 × 0.8	1.5 × 1.5	1.2 × 1.2
Detector	Xe	Xe	Xe	Xe	Xe	Xe	Xe	$CdWO_4$	Xe	Xe	Xe	scint.[a]
X-ray	Pulse	Series	Series	Series	Pulse	Pulse	Series	Series	Series	Pulse	Pulse	Pulse
Pulse width (ms)	3.7	—	—	—	3.0 2.0	2.0	—	—	—	2.2	2.5	B: 3.0[b] H: 2.6[c]
Pulse interval (ms)	10	—	—	—	15	5	—	—	—	7.5	7.5–7.3	5–9.7
Gantry size (mm)	600	550	640	700	600	600	600	620	600	600	600	700
Scan angle	360°	360°	360°	360°	360°	360°	360°	360°	360°	360°	360°	360°, 240°
Scan method	R-R	R-R	R-R	R-R	R-R	R-R	R-R	N-R	R-R	R-R	R-R	R-R

[a] Scintillator.
[b] B = body.
[c] H = head.

current and type of added filter, calibration of the dosimeters was performed for X rays from the KXO-12 unit (Toshiba Corporation) with the same technical parameters as those for the CT scanners in question. The UD-170A TLDs were calibrated in the field of useful X-ray beams and the UD-110S TLDs outside the field at various distances from the X-ray beam axis in a rectangular Mix Dp phantom with a base 20 cm × 50 cm and a height of 20 cm. In the calibration, the exposure at the position of a TLD in the phantom was determined with an ionization chamber which is traceable to the national standard at the Electrotechnical Laboratory in Tsukuba.

Determination of beam dose profile

For the comparison of the output from various CT scanners, the dose profile, defined as the dose distribution on the central line of the scan plane, was determined with the UD-170A TLD rods arranged in full contact, so that no clearance was left behind them, and formed into an equivalent rectangular TLD assembly, 12 mm × 30 mm including thicknesses of glass tubes. The TLD assembly was placed on a foam plastic board to reduce scattering of radiation and was exposed to a single scan beam with the 7th TLD rod fitted to the centre of the scan plane. The dose profile was determined for each scanner using the technical parameters of a lower abdomen examination.

Determination of organ or tissue doses

In order to calculate the effective dose equivalent recommended by the ICRP, the following organ or tissue doses were determined experimentally (ICRP, 1977).

(a) Basic organ or tissue: the thyroid, the lung, the breast, bone surface, bone marrow, gonads (male: testis, female: ovary).
(b) Remaining organs or tissue: five organs or tissues of the remainder receiving the highest dose equivalents, according to the present paper: stomach, liver, large intestine, rectum and bladder.

According to the ICRP recommendation, the brain or salivary glands might be appropriate as one of the remaining organs or tissues for the head CT examinations. In this paper, the organs or tissues having the highest probability of fetal radiation-induced cancers were adopted as the remainders for the calculation of the effective dose equivalent. For the investigation of non-stochastic effects from CT examinations, the doses to the skin and eye lens were determined. The positions of the organs or tissues in the Rando woman phantom were determined on the basis of anatomical pictures taken with CT images by Gambarelli et al (1977). The organ or tissue doses were measured with the TLD rods put in the holes which were made at the corresponding positions of organs or tissues. In the determinations of organ or tissue doses, the number of scans was as follows for all the CT scanners of interest, with the exception of the L type in Table I.

(a) The head CT examination involved nine slices; three slices with a thickness of 5 mm and an incremental distance of 10 mm and six slices with a slice thickness of 10 mm and an incremental distance of 10 mm from the orbitomeatal line (OM-line) upward.
(b) The chest CT examination involved 16 slices with thickness of 10 mm and an incremental distance of 15 mm directed from the xiphoid process to the head.
(c) The upper abdomen CT examination involved 13 slices with a thickness of 10 mm and an incremental distance of 10 mm directed from the xiphoid to the legs.
(d) The lower abdomen CT examination involved 12 slices with a thickness of 10 mm and an incremental distance of 10 mm directed from the upper limit of the pubic bone to the head.

The slice thicknesses for the Type L scanner were 4 mm as opposed to 5 mm in other scanners, and 8 mm as opposed to 10 mm.

The mean bone marrow doses were calculated using a formula presented by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 1972) and the data on the distribution of red bone marrow (Miyakawa, 1965) in the body as given in Table II. The ICRP recommended that the radiosensitive cells in bone were identified as the endosteal

Table II. Distributions of red bone marrow and bone minerals in a Japanese population

Bone	Red bone marrow		Bone minerals	
	Weight (g)	Fraction	Weight (g)	Fraction
Skull	55.6	0.072	663.0	0.179
Mandible	3.7	0.005		
Clavicle	5.6	0.007	44.0	0.012
Scapulae	16.7	0.022	113.0	0.031
Sternum	20.6	0.027	18.5	0.005
Cervical vertebrae	22.2	0.029	51.5	0.014
Thoracic vertebrae	101.0	0.132	156.5	0.042
Lumbar vertebrae	85.6	0.112	128.0	0.035
Sacral vertebrae	65.8	0.086	72.5	0.020
Ribs	104.5	0.136	368.5	0.073
Ilium	170.2	0.222	317.0	0.085
Femur	87.1	0.144	676.0	0.185
Patella			24.5	0.007
Tibia			383.5	0.104
Fibula			90.0	0.024
Feet			198.0	0.053
Humerus	27.9	0.036	237.0	0.064
Radius			75.0	0.020
Ulna			94.0	0.025
Hand			89.5	0.024
Total	766.5	1.000	3700.0	1.000

and the epithelial cells on bone surfaces, and that an average should be calculated over tissue up to a distance of 10 μm from the relevant bone surfaces. In practice, however, it is tedious and time-consuming to calculate the absorbed dose on bone surfaces according to the ICRP recommendation. Assuming that the number of targets in relation to the radiation induced cancer will be dependent on a fraction of bone minerals distributed in the whole skeleton, the doses measured with TLDs at various sites in the phantom were weighted by the fraction of bone minerals (Tanaka, 1981) as given in Table II for the determination of doses on bone surface.

The other organ or tissue doses were determined with the TLDs in the phantom. The effective dose equivalent, H_E, was calculated according to the ICRP recommendation,

$$H_E = \sum_T W_T H_T \qquad (1)$$

where W_T is the weighting factor recommended by ICRP publication 26.

Determination of surface dose on patients

The dose on the surface of phantom was determined with the TLD placed at a central line of the third scan beams for all the CT scanners used.

Results

Determination of Beam Dose Profile

Figure 1 shows relative dose profiles for a single scan. In Fig. 1, the letters indicate the CT scanner measured. The dose profiles were determined with the TLDs arranged in full contact so no clearance was left. These measurements were carried out free in air at the isocentre of the CT head. For the comparison of peak doses for different types of CT scanner, the measured values were normalized for a standard value at 120 kV of tube voltage, 500 mAs and 70 cm between focus and isocentre. The resultant normalized values are given in Table III. The normalized peak doses ranged from 8 to 23, depending on the type of CT scanner.

Organ or tissue doses

In the determinations of organ or tissue doses, the conversion of exposure to absorbed dose factor used was 0.939 for soft tissue and 2.94 for bone (ICRU, 1970). These values were determined on the basis of experimental results in which the effective energy of X rays from CT scanners ranged from 54 to 62 keV, with the average energy of 60 keV. The resultant organ or tissue doses are given in Tables IV–VII. The effective dose equivalents from CT examinations are also given in Tables IV–VII, which were calculated with Equation (1) assuming the quality factor of the X rays is unity. Table IV and VII were simplified by quoting maximum, minimum and median doses. They were selected to compare with the value of the effective dose equivalents.

The doses to the eye lens are given in Table IV. The doses at the surface of the phantom are given in Tables IV–VII. For the surface doses, the maximum and

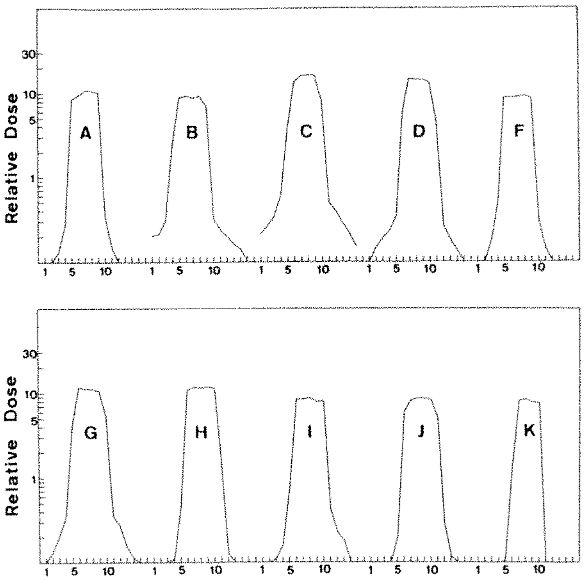

Figure 1. Dose profiles for a single scan. The letters (A–K indicate the type of scanners given in Table I. (The figures on the axis of abscissa show the number of TLDs for each scanner).

Table III. Normalized peak dose calculated from beam profile shown in Fig. 1

Scanner	A	B	C	D	F
Tube voltage	120	120	120	120	120
mAs/scan	533	259	390	420	300
Dose	10.10	8.81	17.23	13.24	8.76
Normalized dose	11.76	9.57	12.43	12.76	13.98
Scanner	**G**	**H**	**I**	**J**	**K**
Tube voltage	120	120	120	120	120
mAs/scan	440	200	360	396	450
Dose	11.59	11.59	8.38	8.69	8.20
Normalized dose	12.61	23.18	8.55	8.06	9.11

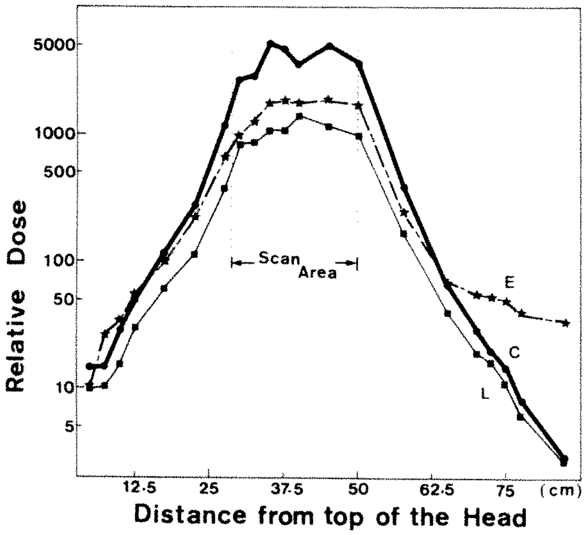

Figure 2. The dose distribution in the phantom for chest CT examination. The letters C, E and L indicate the type of scanners given in Table I.

average values in the primary beams for an examination are given in the tables.

Discussion

As shown in Fig. 1, the peak doses at the isocentre of the CT head varied considerably from one scanner to another. Poletti et al (1984) have measured dose distributions in a cylindrical CT phantom. They have reported that there were differences of 200% or 300% at the peak doses. Assuming that the peak dose was proportional to the square of tube-voltage, tube current, exposure time and the square of the distance between the focus and the detector, the measured doses shown in Fig. 1 were normalized to the values at the tube voltage of 120 kV, the mAs value of 500 and a distance of 700 mm, using those factors reported by the manufacturer of the corresponding CT scanner. The resultant values ranged from about 8 to about 23 with a mean value of 12.20. These differences may be due to the differences in some factors, such as the size of the focus, the effective atomic number of the target material, quality of the filter materials and so on. Unfortunately, the information on these factors was not available from the manufacturers of the CT scanners.

The absorbed doses received by the organs or tissues that lie within the field of the primary X-ray beams varied considerably from one scanner to another, depending on the peak doses for each scanner. The organ or tissue doses outside of the primary X-ray beams depend on the construction of each CT scanner. For the chest scan, the doses to ovary and rectum by the Scanner E were extremely large compared with the doses from other scanners. Figure 2 shows the doses at the various sites where the bone marrow doses were determined with the TLDs for the chest CT examination. As is evident from Fig. 2, the organ or tissue doses from Scanner E are larger than the doses from the others. This may be due to large scattered doses from the Type E collimator system.

The entrance dose of the phantom can generally be used for the comparison of the performance of CT scanners. McCrohan et al (1987) have compared the entrance doses for a typical adult head scan for 250 CT systems. They showed that the average dose at the centre of a series of head scans ranges from 22 mGy (2.2 rad) to 68 mGy (6.8 rad). The present measurement showed the entrance doses in nine scans were from 18 to 80 mGy. Since the organs or tissues which lie within the abdominal region were selected as remainders in the determination of effective dose equivalents, present values from the head scanning procedures might be underestimated. For example, for the CT scanner of G-type, the effective dose was estimated to be 1.2 mSv when the sublingual gland, the parotid gland, the submaxillary gland, the stomach and the large intestine were selected as the remainders in the determination of effective dose equivalent. Huda et al have reported an effective dose equivalent of 2.13 mSv for the pelvis CT examination with an EMI 5005 scanner. This value was considerably smaller than the present data. This may be because of the difference in rotation angles between the EMI 5005 (180°) and other CT Scanners (360°) used in this study.

Scanners C, G and H were designed to obtain potentially higher maximum output of X rays. Sometimes

Table IV. Organ or tissue doses from head CT examination by type of CT scanner

Scanner		A (Minimum)	C (Maximum)	Mean
Tube voltage (kVp)		120	120	
mAs/scan (mAs)		533	520, 400	
Organ doses (mGy)				
Ovary		0.002	0.003	0.003
Testis		0.002	0.002	0.002
Breast		0.042	0.125	0.107
Red bone marrow		0.704	2.072	1.454
Lung		0.030	0.122	0.080
Thyroid		0.236	0.788	0.548
Bone surface		4.34	12.74	8.95
Others:				
Stomach		0.008	0.024	0.020
Liver		0.009	0.028	0.021
Large intestine		0.003	0.004	0.004
Rectum		0.003	0.004	0.003
Bladder		0.002	0.002	0.003
Effective dose equivalent (mSv)	Male	0.234	0.692	0.489
	Female	0.234	0.692	0.489
Eye dose (mGy)		8.74	47.2	22.40
Surface dose (mGy)	Maximum	18.18	81.10	39.8
	Average	17.47	60.90	32.1

Table V. Organ or tissue doses from chest CT examination by type of CT scanner

Scanner		A	B	C	D	E	F	G	H	I	J	K	L	Mean
Tube voltage (kVp)		120	120	120	120	120	120	120	120	120	120	120	125	
mAs/scan (mAs)		533	259	390	340	360	300	440	200	360	330	300	350	
Organ doses (mGy)														
Ovary		0.055	0.042	0.098	0.070	0.437	0.121	0.101	0.055	0.079	0.070	0.051	0.078	0.105
Testis		0.019	0.011	0.025	0.027	0.384	0.030	0.031	0.017	0.026	0.027	0.019	0.024	0.053
Breast		11.08	8.89	39.6	18.95	10.23	20.0	12.24	15.37	8.72	13.28	12.10	20.3	15.90
Red bone marrow		4.83	4.43	11.48	6.12	5.04	6.76	6.75	4.60	5.91	4.52	3.94	3.87	5.69
Lung		18.41	12.64	35.0	21.1	17.35	21.7	24.7	16.96	21.2	17.42	13.39	15.32	19.60
Thyroid		1.453	1.501	3.00	1.884	2.23	1.580	2.59	1.614	2.03	1.823	1.363	1.192	1.855
Bone surface		6.94	6.35	17.19	8.94	7.35	9.61	10.12	6.66	8.49	6.76	5.57	6.06	8.34
Others:														
Stomach		8.99	5.96	16.59	10.89	7.58	18.59	8.86	5.92	7.72	6.81	6.20	6.19	9.19
Liver		7.66	5.68	15.26	9.43	7.12	20.2	8.63	5.55	7.12	5.95	6.69	8.18	8.96
Large intestine		0.080	0.065	0.144	0.108	0.549	0.163	0.140	0.080	0.114	0.103	0.078	0.110	0.145
Rectum		0.061	0.041	0.098	0.068	0.529	0.124	0.103	0.058	0.088	0.072	0.060	0.079	0.115
Bladder		0.038	0.031	0.066	0.056	0.421	0.124	0.072	0.041	0.058	0.058	0.053	0.068	0.091
Effective dose equivalent (mSv)	Male	5.72	4.33	14.05	7.67	5.58	9.11	7.06	5.84	5.79	5.67	4.89	6.45	6.85
	Female	5.73	4.34	14.07	7.69	5.59	9.14	7.08	5.85	5.80	5.68	4.90	6.46	6.86
Surface dose (mGy)	Maximum	21.7	19.79	62.8	31.5	16.48	26.0	28.9	20.4	27.2	21.1	18.64	22.7	26.4
	Average	20.5	15.20	57.2	27.5	15.02	23.3	24.7	15.37	23.7	16.64	15.02	18.61	22.7

Table VI. Organ or tissue doses from upper abdomen CT examination by type of CT scanner

Scanner		A	B	C	E	F	G	H	I	J	L	Mean
Tube voltage (kVp)		120	120	120	120	120	120	120	120	120	125	
mAs/scan (mAs)		533	259	390	360	300	440	200	360	396	350	
Organ doses (mGy)												
Ovary		0.464	0.416	0.850	0.413	0.726	1.039	0.493	0.640	0.663	0.440	0.614
Testis		0.067	0.040	0.083	0.214	0.126	0.156	0.066	0.096	0.109	0.073	0.103
Breast		0.548	0.386	1.217	1.249	0.675	1.109	0.456	0.761	0.797	0.584	0.778
Red bone marrow		1.670	1.535	3.66	2.30	2.45	2.61	1.457	2.27	2.26	1.382	2.16
Lung		1.224	0.998	2.90	2.41	1.606	2.19	1.08	1.495	1.645	1.225	1.678
Thyroid		0.073	0.048	0.146	0.678	0.134	0.190	0.069	0.134	0.133	0.104	0.171
Bone surface		1.800	1.640	3.95	2.78	2.65	2.88	1.59	2.47	2.45	1.538	2.37
Others:												
Stomach		25.6	15.730	47.6	26.3	29.7	36.7	17.93	24.8	27.4	17.57	26.9
Liver		23.1	17.16	51.8	24.8	35.0	34.0	19.93	28.1	26.2	16.91	27.77
Large intestine		0.725	0.693	1.507	0.653	1.165	1.736	0.788	0.998	1.023	0.665	0.995
Rectum		0.312	0.259	0.749	0.273	0.470	0.690	0.303	0.432	0.403	0.349	0.424
Bladder		0.302	0.259	0.578	0.334	0.487	0.744	0.329	0.432	0.456	0.290	0.421
Effective dose equivalent (mSv)	Male	3.51	2.47	7.24	4.05	4.71	5.30	2.80	3.95	4.02	2.61	3.67
	Female	3.61	2.56	7.43	4.10	4.86	5.52	2.90	4.09	4.16	2.71	3.78
Surface dose (mGy)	Maximum	29.2	21.3	72.1	34.0	38.2	52.3	27.0	29.4	28.8	26.8	35.9
	Average	28.9	17.9	55.4	22.3	30.8	37.0	20.5	25.3	23.0	24.7	28.6

Table VII. Organ or tissue doses from lower abdomen CT examination by type of scanner

Scanner		L (Minimum)	C (Maximum)	Mean
Tube voltage (kVp)		125	120	
mAs/scan (mAs)		350	390	
Organ or tissue doses (mGy)				
Ovary		8.68	27.10	15.14
Testis		0.532	1.622	1.036
Breast		0.125	0.144	0.112
Red bone marrow		3.49	9.51	5.60
Lung		0.123	0.144	0.130
Thyroid		0.031	0.021	0.027
Bone surface		4.35	11.32	6.71
Others:				
Stomach		0.364	0.595	0.466
Liver		0.393	0.611	0.487
Large intestine		11.31	34.5	19.23
Rectum		4.54	16.99	9.92
Bladder		5.04	17.76	10.56
Effective dose equivalent (mSv)	Male	2.02	6.17	3.61
	Female	4.05	12.53	7.13
Surface dose (mGy)	Maximum	20.6	53.9	30.3
	Average	18.11	47.8	23.3

manufacturers recommend to their users technical factors of CT scanning in an attempt to get better density resolution. However, the recommended technical factors may introduce unnecessarily higher patient doses because of the higher X-ray output compared with the normal technique. From the point of view of radiation protection for patients, an optimum factor for CT examinations should be decided by considering not only the image quality but also the absorbed dose or effective dose equivalent resulting from CT procedures. This can be achieved only by consensus through discussion about optimal dose among manufacturers, medical physicists and radiologists who actually read films.

Conclusion

The result of dose determinations from various types of CT examinations showed that there was a marked variation in organ or tissue dose depending on the CT unit even for the same type of examination. Consequently, the resultant effective dose equivalents by type of CT examination ranged from 0.23 to 0.7 mSv with a mean value of 0.5 mSv for the head examinations, 4.3 to 14 mSv with a mean value 7 mSv for the chest, and 2.5 to 7.4 mSv with a mean value 3.7 mSv for the upper abdomen, respectively. For the lower abdomen examinations, there was a wide discrepancy depending on sex: the effective dose equivalents ranged from 2 to 6 mSv with a mean value of 3.6 mSv for males and 4 to 12.5 mSv with a mean value of 7 mSv for females, respectively. As for the optimization of radiation protection to the patients, the wide discrepancy in the effective dose equivalent depending on the type of CT unit should be seriously considered when choosing a CT unit, together with the determination of technical factors for the CT examinations.

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Carcinoma of the breast: measurement and the management of treatment

I. The value of the data

By *C. W. D. Cheung, MSc and A. E. Johnson, FRCS, FRCR

Breast Study Centre, Mount Vernon Hospital, Northwood, Middlesex

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Abstract. This is the first of a series of papers in which we shall explore some insights into the biological changes which accompany the treatment of human tumours which may be obtained through estimation of volume changes in relation to treatment. We have adopted a working hypothesis that regression slopes reflect the composition of individual tumours and, indirectly, their intrinsic growth rate rather than the effectiveness of treatment. The breast has proved to be a suitable site for measurement and our interpretation of the results has led to the development of a new style of management for carcinoma of the breast: measurement based sequential therapy (MBST). In this paper the method of measurement and detailed statistical evaluation of the quality of the data from 262 patients (263 tumours) is presented. Exponential regression lines have been fitted to describe volume changes in relation to treatment by radiation, chemotherapy and hormones. A simple classification of steepness of slopes is introduced.

The work which will be reported was initiated in 1974 by the late Dr R. H. Thomlinson as an extension into the clinical field of his laboratory investigations using a fibrosarcoma in the rat. He had demonstrated that sufficient doses of radiation to produce shrinkage, administered in different conditions of oxygenation to transplants of the same tumour, consistently reproduced the same regression line; whereas the treatment of tumours of diverse histology produced different lines. The relative effectiveness of individual treatments was apparent, in the experimental situation, in the differences in the time delay before regrowth of the tumour (Thomlinson, 1960; Thomlinson & Craddock, 1967).

The regression line reflecting shrinkage was defined as the "resorption" slope. Resorption is an apposite name because some of the substance of the tumour must be removed through the circulation before a decrease in size can be observed. The rate of removal was expected to depend upon the natural lifetime of the non-clonogenic tissue components: rapid for poorly differentiated cells and slow for stroma such as collagen, with a full range between.

Since what is removed must have grown, Thomlinson advanced the hypothesis that, in response to effective treatment, each individual human tumour should also display a characteristic resorption slope which would reflect its unique histological composition and therefore, indirectly, be informative about its intrinsic growth rate; the steepness of the slope alone would not define the effectiveness of treatment. We further postulated that delay in regrowth might be expressed in terms of the characteristic slope to enable comparisons between treatments.

The first problem was to achieve a satisfactory method of measurement. Preliminary attempts by Thomlinson to measure human tumours that were being treated by colleagues in the Regional Centre for Radiotherapy and Oncology led to the choice of carcinoma of the breast for further investigation, by virtue both of its accessible site and of the frequency of its occurrence.

The enormous variety in both histology and growth rate in breast cancer (Bloom & Richardson, 1957; Heuser et al, 1979) carried the implication that a wide range of characteristic slopes would be anticipated. An extension of the original hypothesis was that establishment of this range would enable a more satisfactory classification of breast tumours according to their intrinsic behavioural properties. Measurement of the individual slope should then assign new cases to appropriate management in contradistinction to the present *post hoc* staging procedures.

This first paper describes the technique of measurement, the method of estimation of tumour volumes and the regression analysis of the data ("regression" is used in the statistical sense, representing either growth or resorption of tumours). The errors inherent in the foregoing are considered and, finally, regression lines associated with a variety of treatments are presented.

Collection of the data

At the beginning, measurements were made of breast cancers for which local radiotherapy was being administered by colleagues. The primary goal was to establish the method; the measurers were not involved in the clinical management. Inferences drawn from these first regression data resulted, in 1975, in the introduction,

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*Present address: CRC Gray Laboratory, Mount Vernon Hospital.

Address for correspondence: Dr A. E. Johnson, Breast Study Centre, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN.

prior to radiation, of what has since been dubbed "neo-adjuvant" chemotherapy (Frei, 1982) in collaboration with Dr Paul Strickland (Thomlinson, 1977). By 1979 it had become clear that the regression data could be used to control the day-to-day management of breast cancer by systemic therapy. Therefore, in collaboration with Mr J. E. L. Sales at Mount Vernon Hospital and Mr S. J. Cox of Watford General Hospital, we opened The Breast Study Centre, a clinic dedicated to the management of new, primary breast cancer. The cornerstones of management were that systemic treatment would be given first and that each individual patient's course would be controlled through measurement of their primary tumour: "measurement based sequential therapy" (MBST). Since these regression data would be new, observational information uniquely applied, no attempt was made to select or stratify new patients. No measurable case was refused (including those with demonstrable metastases) but deeply ulcerated tumours where the bulk of the mass had been shed were rejected as unsuitable for attempted estimations of volume. In every case the diagnosis had been confirmed histologically, usually by drill biopsy. Thus our measurement series covers a range of presentation, from advanced cases referred for palliation to "early" tumours from the general surgical clinic. The patients having local radiotherapy as their first management had been selected by their referring clinician for adverse features, whereas the MBST series may be claimed to be representative but not comprehensive of breast cancer in the catchment areas of two district hospitals (one surgeon from each hospital collaborating).

The measurements, begun in 1974, continued until 1987; the whole series comprised 262 patients (263 tumours). The ages of these patients were normally distributed about a mean of 60 years with a range from 25 to 86 years (Fig. 1). The presenting diameters of the tumours were log normally distributed with a geometric mean of 46 mm and a range from 14 to 161 mm (Fig. 2).

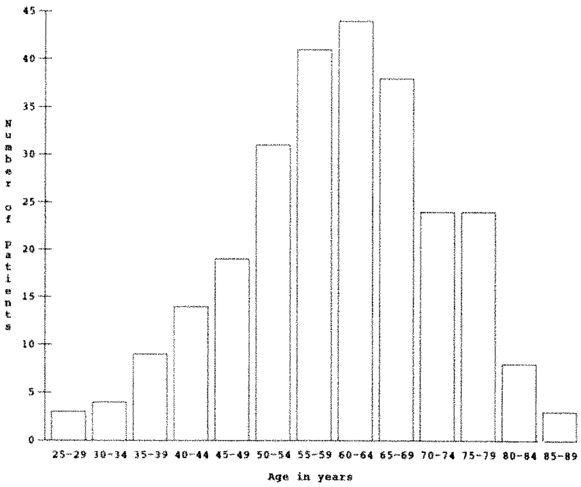

Figure 1. Age distribution of the 262 patients.

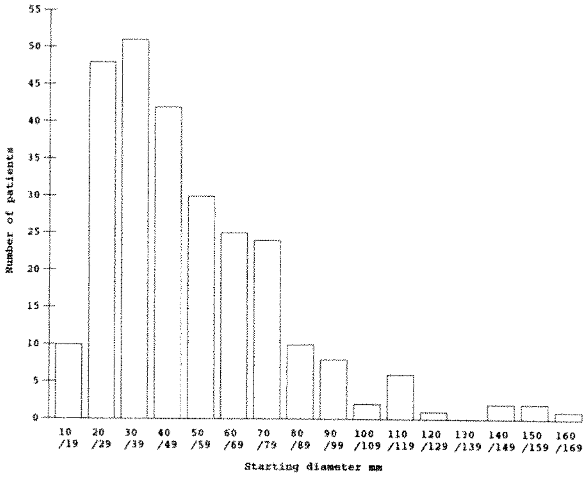

Figure 2. Distribution of starting diameters.

There were 44 (17%) premenopausal, 193 (74%) postmenopausal and 25 (10%) perimenopausal patients. Perimenopausal patients were defined as those in the 45–55 age group who were still menstruating but were experiencing menopausal symptoms. It was not possible to estimate hormone levels.

Measurement

Four diameters of each tumour were measured at intervals of approximately 45° (Fig. 3), recording to the nearest millimetre using engineers' callipers made of

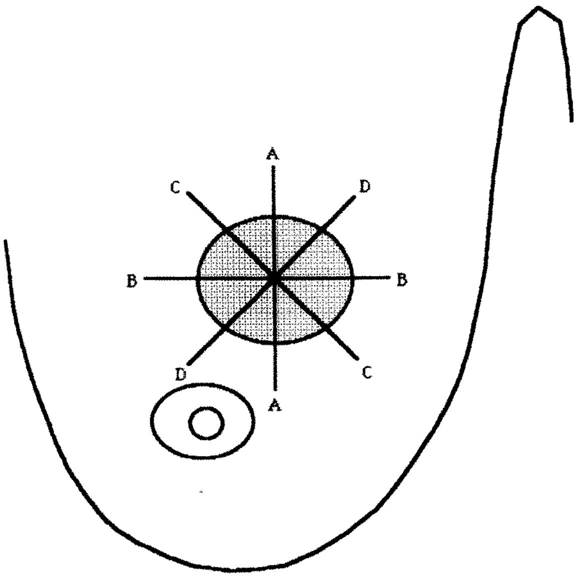

Figure 3. Diagram showing planes of measurement which were recorded in the order AA, BB, CC, DD. The patient lay supine with sufficient elevation of the head for comfort and the arm positioned for best exposure. The same posture was adopted in successive examinations.

plastic. In order that no external bias should be introduced, new measurements were made before seeing any previous values or the current ones of colleagues, each observer writing their figures privately in separate loose-leaf books kept for the purpose. At first, one set of four measurements was made but, from January 1982, a second full set of measurements was made, as a check, by each observer immediately after all had completed their first set. Where available, the mean of each of the separate diameters from the two sets was used in calculation of the overall mean tumour diameter for each observer and the eight observations were treated as though they were four in all statistical tests.

Measurements were made at every attendance, generally at weekly intervals for chemotherapy treatments, compared with five times weekly for the majority of radiotherapy patients, who received daily fractionation. Reduction in the frequency of visits occasioned by follow-up after radiotherapy, taking place at a peripheral hospital, resulted in sparse data unsuitable for the fitting of regression lines.

Measurers

Measurements have been made by a total of 13 observers. Observer 1 was present throughout; Observer 4 was present during the last 6 years, combining with all except Observer 2. The rest of the observers were appointed in temporal order and their measurements coincided with those of Observers 1 and 4 but with few or no others. Observers 6, 7, 9, 11 and 13 were present for a short time, making relatively few measurements.

Evaluation of the measurements

Before these measurements of diameter may be used to estimate tumour volumes, we must examine the errors associated with the method, which relate both to the tumours and to the observers. If the tumours had been uniformly spherical, if they had shrunk or grown symmetrically and if the measurers were consistent and in agreement with each other over the whole range of diameters, then the daily combined mean diameters and their standard errors might be used directly to calculate volumes for regression analysis. These caveats are addressed below.

We have used the General Linear Models (GLM) procedure supplied in the SAS* package for the CRC Gray Laboratory MicroVAX computer in our analyses. Where not otherwise specified, the cut-off value for significance is taken as $p<0.05$.

Tumours

It is not possible to estimate the absolute size of these tumours by external calliper measurement because of their covering of skin, fat and other breast tissues. Also, we could not measure the anteroposterior diameter. Tumours exhibited a variable degree of ellipticity, some changed in shape during growth or shrinkage and often, a large, elliptical tumour would become a small, spherical one. Apparent changes with time will be influenced by alterations in the quantity of subcutaneous tissue and in the degree to which the tumour is compressed during measurement; depending upon its initial size and site, shrinkage may make the margins more clearly defined or more inaccessible. Every effort was made to obtain the first measurements before the biopsy; this policy was not always successful, so some presenting diameters may show spurious enlargement due to bruising.

Individual observers

Observers generally achieved a consistent technique within 3–4 weeks of joining: it was our custom to discard early measurements of new observers until they had developed this internal consistency. The second set of measurements, where taken, was, apart from the discovery of errors in reading and recording the calliper dial, highly dependent upon the first set. It was not practicable to make multiple calliper estimations on the same day in an out-patient clinic, so an assessment of within observer repeatability cannot be made.

There was a trend towards smaller tumours later in the series so that the changing observer sequence means that different observers have measured a different range of tumours (Table I). The effect of the wide range of diameters was investigated for individual observers in a sample composed of the data from the fourth measurement occasion for each patient. The fourth observation was chosen to avoid the earliest measurements which might be influenced by a biopsy or inconsistencies in dealing with a new patient and before any tumours had disappeared (no slope being fitted to fewer than four points). The distribution of the mean diameters was tested for normality and the diameters were plotted against their standard errors. Since a normal distribution was not found in every case, the Spearman rank correlation coefficient was used to test the relationship between these parameters.

The distribution of diameters was non-normal in the cases of Observers 1, 3, 4 and 9. These observers, together with Observers 2, 5 and 8, showed a positive correlation (*i.e.* increasing standard error with larger diameters) between mean diameter and standard error which may be removed for all save Observer 1 by log transformation (Table I).

Differences between observers

Is it permissible to combine the measurements of a number of observers in order to estimate volumes? Because of the changing range of diameters and the temporal sequence of observers, the best critical evaluation of the quality of the combined measurements seemed to lie in investigating the differences between pairs of observers, in the manner suggested by Altman and Bland (1983) for comparison of two experimental methods of measuring the same physical property. Observer 1 may be compared with all other observers and Observer 4 with all except Observer 2.

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*SAS: Statistical Analysis Systems Institute Inc.

Table I. Range and distribution* of diameters, number of samples, geometric mean diameter and its correlation with the standard error for each individual observer

Observer	Range (mm)	N	Number	Mean (mm)	Untransformed		Log transformed	
					r	*p*	*r*	*p*
1	10–160	–	263	41	0.71	0.0001	0.22	0.0004
2	21–143	+	62	58	0.65	0.0001	−0.08	0.56
3	20–159	–	89	50	0.49	0.0001	−0.01	0.95
4	12–101	–	130	32	0.58	0.0001	−0.01	0.91
5	12–101	+	19	40	0.76	0.0002	0.18	0.47
6	11–83	+	9	40	0.50	0.17	0.15	0.70
7	13–80	+	10	38	0.30	0.41	−0.36	0.31
8	16–52	+	45	28	0.58	0.0001	0.17	0.28
9	15–81	–	8	29	0.71	0.047	0.45	0.26
10	14–50	+	26	27	0.31	0.12	−0.35	0.08
11	22–34	+	6	27	0.60	0.21	−0.43	0.40
12	14–43	+	25	26	0.03	0.90	−0.35	0.09
13	12–46	+	9	24	0.18	0.65	−0.42	0.27

*A normal distribution is indicated by + in the column under "N".

For each observer pairing we examined:

1. the range of tumour diameters over which measurements were made;
2. the distribution of differences between observers;
3. the 95% boundaries of those differences;
4. the correlation between inter-observer differences and the mean diameters measured.

Results

1. A steady fall in the range of tumour diameters measured by the sequence of observer pairs was seen. This is illustrated graphically in Fig. 4.
2. In examining the differences between observers we have used the same data set as in the investigation of the correlation between mean diameters and their standard errors for individual observers but have dealt with each of the four diameters separately in order to remove ambiguity due to ellipticity. The distributions of the differences were tested for normality. In 14 of the 22 pairings the distributions of differences were non-normal (Table II). However, in only one example (Observers 1 *versus* 3) was the distribution highly non-normal. Taking into account the large number of observations, we therefore assumed normal distributions for the purpose of calculating the approximate 95% boundaries of the differences.
3. We may not enter the normal distribution tables at a value equivalent to $p = 0.05$ since, by re-using some

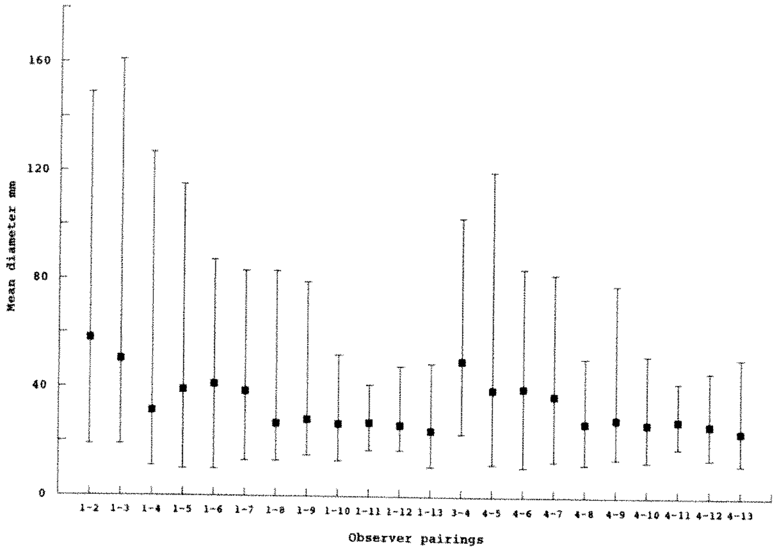

Figure 4. The range of diameters measured by each observer pair, together with their overall geometric mean (filled squares).

Table II. Range, number of samples and mean diameters measured by observer pairs with distribution* and 95% confidence limits of their differences

Observer	Observer 1					Observer 4				
	Range (mm)	Number	Mean (mm)	N	95% (mm)	Range (mm)	Number	Mean (mm)	N	95% (mm)
2	19–149	248	58	–	±13					
3	19–161	352	50	–	± 8	23–103	72	50	–	±15
4	11–127	520	31	–	±13					
5	10–115	76	39	–	±11	12–120	76	39	+	±13
6	10–87	36	41	–	±10	11–84	36	40	+	±10
7	13–83	40	39	+	± 9	13–82	40	37	+	± 9
8	13–53	180	27	+	±12	12–51	180	27	+	±13
9	13–79	32	28	–	±20	14–78	28	29	–	±21
10	13–52	104	27	–	±11	13–52	100	27	–	±12
11	17–41	24	27	+	±13	18–42	20	28	+	±10
12	13–48	100	26	–	±18	14–46	100	26	–	±15
13	11–49	36	24	–	±11	12–51	36	24	–	±11

*A normal distribution is indicated by + in the columns under "N".

measurements in comparisons between Observers 1 and 4 and others, we have effectively made many tests, and p (overall) would be larger. It is therefore necessary to apply a more stringent procedure and we followed the suggestion of Altman and Bland in using $z=\pm 2.836$ instead of ± 1.96 (*i.e.* as for $p=0.005$ for each of 10 individual tests) in the estimation of the 95% boundaries. The range for all observers is wide, from ±8 mm to ±21 mm, averaging ±13 mm (Table II). For each observer pair, we drew a bargraph of the distribution of their differences and the difference on each measurement occasion was plotted against the mean diameter for that day; a typical set of graphs is shown in Fig. 5.

4. We have used the Spearman rank correlation coefficient because the differences are not all normally distributed. In Table III we see that most observer pairings, where over 100 comparisons may be made, show no correlation between differences and mean diameter. Observers 6 and 9 did show significant correlations in all their pairings, but the number of comparisons achieved was low, as it was for the combination 1–11. Others whose correlations reached significance actually produced relatively small correlations.

Thus there was a range of differences between observers but, once sufficient observations were made, the *differences* were generally independent of diameter.

Discussion

Calliper measurements of breast tumours are affected by the site of the tumour in relation to the breast disc, its depth from the surface and the degree of compression applied by the observer. The microscopic margins of a tumour are usually diffuse with a varying amount of stromal reaction and oedema. A sole patient in our series had an encapsulated tumour. "Diameter"

Table III. Correlation of differences and mean diameters between Observers 1 and 4 and others

Observer	Observer 1			Observer 4		
	Number	r	p	Number	r	p
2	248	0.10	0.14			
3	352	0.07	0.18	72	0.08	0.50
4	520	−0.05	0.28			
5	76	0.28	0.016	76	0.22	0.056
6	36	−0.55	0.0005	36	−0.49	0.0024
7	40	−0.29	0.07	40	−0.08	0.62
8	180	0.10	0.20	180	0.23	0.002
9	32	−0.55	0.0012	28	−0.57	0.0016
10	104	0.30	0.0019	100	0.21	0.041
11	24	0.43	0.034	20	0.42	0.062
12	100	0.24	0.12	100	0.29	0.0038
13	36	0.25	0.15	36	−0.15	0.38

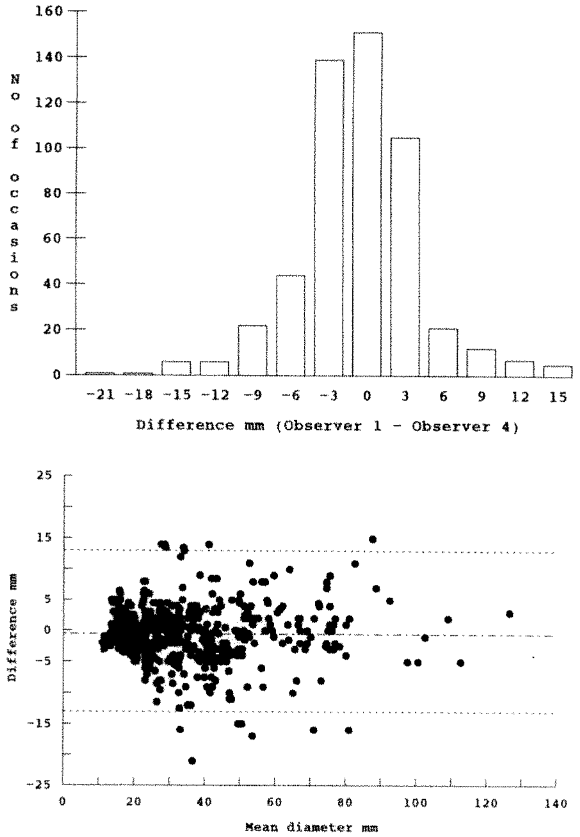

Figure 5. Differences between observers presented as recommended by Altman and Bland. The upper figure shows the distribution of differences between one pair of observers (1 and 4) in a sample of data taken on the fourth measurement occasion for each patient; each diameter, A, B, C and D, is treated separately. The differences are distributed in 3 mm wide intervals centred upon the numbers shown on the x-axis. In the lower graph, these differences have been plotted against the corresponding mean diameter. The central horizontal line shows the overall mean difference (-0.53 mm) and the upper and lower dotted lines the 95% boundary limits of the differences (± 13 mm).

measurements become a composite of central, solid tumour, peripheral, partially compressible tumour and surrounding normal tissue, which may be tense or slack. Thus the changes recorded are relative.

Elliptical tumours will generate spuriously large errors when the diameter measurements are combined, but most of the correlation of standard error with mean diameter seen for individual observers may be removed by log transformation of the diameters. The absence of correlation between differences and mean diameters suggests that, on the whole, the observers are consistent. This is important, since the range of diameters measured by different observer pairs was wide.

Thus we found that the tumours were not uniformly spherical, did not shrink and grow symmetrically and that, although individual observers were consistent over

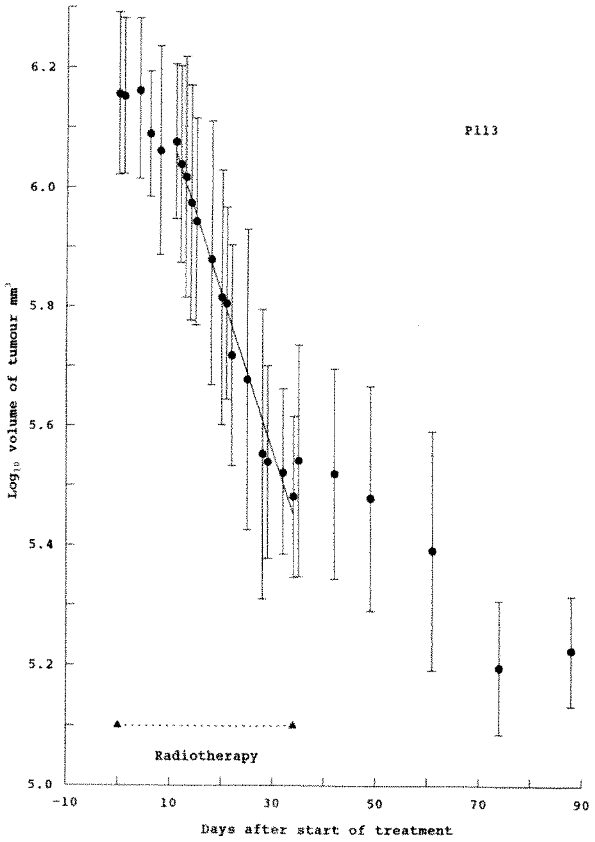

Figure 6. Log_{10} volume of one tumour plotted against time showing the mean volume and 95% confidence limits for each measurement day. The equation of the fitted slope is $y = 6.35 + (-0.0264x)$. Volume halving time = 11.4 days, natural logarithm of unsigned slope = -3.63.

the range of diameters measured, they disagreed significantly with other observers. Therefore, we decided to handle the data from each individual observer separately in the regression calculations and to apply weights to the individual data so that excessive significance would not be given to aberrant observations. This does not remove the effect of the absence of an observer who consistently measured above or below the values of colleagues upon the mean value for that day.

It is tempting to try to define the difference in diameter that the various combinations of observers could detect at a stated level of significance. However, since tumours grow and shrink at different rates, a definition based on a standard time interval will combine differences related to the regression slope with observational error (*e.g.* there will naturally be a larger difference for rapidly shrinking tumours compared with slower ones), whereas a standard reduction in size (Hayward et al, 1977) will occur at varying times for different tumours, irrespective of the accuracy of measurement. Our final conclusion was that at least four points on a significant regression slope were required to

Table IV. Final analysis of regression slopes according to their significance and classification by their natural logarithms

Ln slope	Significance					
	Resorption			"Growth"		
	$p < 0.001$	$p < 0.01$	$p < 0.05$	$p < 0.001$	$p < 0.01$	$p < 0.05$
−9.0 up to −8.5	0	0	0	1	0	0
−8.5 up to −8.0	0	0	0	0	0	0
−8.0 up to −7.5	0	0	2	1	0	0
−7.5 up to −7.0	1	0	0	1	0	2
−7.0 up to −6.5	7	2	0	5	6	3
−6.5 up to −6.0	19	3	4	9	5	2
−6.0 up to −5.5	41	5	5	22	8	5
−5.5 up to −5.0	68	6	1	34	10	6
−5.0 up to −4.5	98	5	5	25	11	4
−4.5 up to −4.0	101	12	4	16	6	5
−4.0 up to −3.5	68	9	2	11	4	3
−3.5 up to −3.0	30	6	0	6	0	0
−3.0 up to −2.5	9	0	1	0	1	0
−2.5 up to −2.0	4	0	0	0	0	0

Summary

Significance	$p < 0.001$	$p < 0.01$	$p < 0.05$	Total
Resorption	446	48	24	518
"Growth"	131	51	30	212
Total	577	99	54	730

quantify a change. Policy decisions based on two measurements separated by 1–4 weeks were often reversed when more data became available.

Regression

As a result of the preceding statistical evaluation, the data of individual observers were handled separately. Where more than one set of diameters had been measured, the arithmetic mean of each of the four diameters was first calculated. Log transformation of each diameter was made and these log diameters were then used to calculate the individual observer's geometric grand mean diameter and hence the log volume ($\log_{10}$ mm^3), assuming a spherical shape. Where more than one observer had measured, the mean volume for the occasion was then taken. When the mean log volumes were plotted against time, a zone of exponential regression was usually observed, although this did not always coincide with the beginning of the treatment (Fig. 6).

Regression lines were then fitted to sets of points in relation to different treatments. The starting point of each line was placed as near as possible to the beginning of a new treatment and the end point where the effect appeared complete. Where there was doubt when fitting by eye, several starting and end points would be tried and the steepest, most significant slope selected. A weighted least squares regression was used (Draper & Smith, 1966). The daily volumes estimated from individual observer's data were weighted by the reciprocal of their standard deviation and a preliminary analysis of variance performed. The F statistic obtained from analysis of variance defines linearity with a high degree of significance. Slopes were recorded for $p<0.001$, $p<0.01$ and $p<0.05$, and where $p>0.05$ they were rejected. In this way, the choice of starting and end points of the regression, while remaining in the hands of the operator for trial, does not lead to the fitting of poor quality slopes.

Regression slopes have been fitted to our data in relation to radiation, chemotherapy, hormones and combinations of these three modalities. "Growth" slopes were usually associated with ineffective treatment; there were only 19 slopes reflecting untreated growth.

The average number of data points per line lies between seven and eight and is never less than four. In 157 cases it was possible to fit more than one regression line and for 139 tumours there was more than one resorption slope. In these latter cases we used the weighted least squares regression to examine the following hypotheses: that the separate data sets were best fitted by independent lines, that they were best fitted by parallel lines or that contiguous sets of data were best fitted by a single line. In five cases a single line replaced two separate ones. Four of these related to radiotherapy, where the number of data points was larger and apparent breaks in continuity had been produced by gaps in treatment at weekends or public holidays. In 61 cases, parallel slopes were identified; in seven of these cases there were two sets of different parallel slopes attributable to the same tumour. Table IV enumerates the resulting 730 regression lines fitted for the total of 262 patients (263 tumours).

Eighty-six per cent of the resorption lines and nearly half the "growth" lines are significant at $p<0.001$. The rather unwieldly values for regression slopes ranging from absolute values of 0.132 to 0.00019, when subjected to natural log transformation (ignoring the sign), become a convenient range from 2.03 to 7.96 for resorption slopes and from 2.91 to 8.57 for "growth".

Conclusions

It is possible to obtain regression lines describing the volume changes in breast cancer occurring during and after treatment using engineers' callipers to measure diameters. Despite the variety of observers and types of patient presentation, a consistent picture emerges with time, provided that the relative nature of the measurements is remembered. Two limitations which cannot be improved by statistical manipulations are the varying ellipticity of tumours and the error introduced by the absence of one observer whose measurements, though consistent, are always larger or smaller than the others.

This analysis is presented as the justification for the use of the above detailed set of regression slopes as a data base from which to explore the interpretation of the lines in relation to our original hypotheses.

Acknowledgments

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Selective uptake of toxic nucleoside (^{125}IUdR) by resistant cancer

By Kenneth D. Bagshawe, MD, FRS, Surinder, K. Sharma, MSc, Peter J. Southall, MRCPath, Joan A. Boden, LI. Biol. Geoffrey M. Boxer, FIMLT, *Terence A. Patridge, PhD, Pari Antoniw, MSc and Rosamond B. Pedley, PhD

Cancer Research Campaign Laboratories, Department of Medical Oncology and *Department of Histopathology, Charing Cross and Westminster Medical School, London W6 8RP, UK

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Abstract. We report uptake of a thymidine analogue 125-Iodine-5-iodo-2′-deoxyuridine (^{125}IUdR) by nude mice bearing human xenografts of choriocarcinoma or colonic cancer. When ^{125}IUdR was given alone, uptake by intestinal tissues was 5–10 times greater than by the tumours as measured by tissue γ counting. This ratio was reversed when hydroxyurea or cytosine arabinoside were used as inhibitors of ribonucleotide reductase and were given in combination with 5-fluorouracil or methotrexate to inhibit thymidine synthesis shortly before injecting ^{125}IUdR. Counting the radioactivity in tissues removed 24 hours after ^{125}IUdR gave tumour to highest normal tissue ratios of up to 15:1, but the corresponding nuclear grain counts, which is probably a more reliable indicator of selective uptake into DNA, were in excess of 100:1. The addition of unlabelled IUdR to the regimen only reduced the uptake of ^{125}IUdR when given in relatively large amounts. For this approach to be exploited it is concluded that the tumour must be resistant at the cell level to the inhibitor of DNA synthesis either *de novo* or as a result of prior exposure to it. This inhibitor can then be used to block uptake of the potentially toxic nucleoside analogue by normal renewal tissues while it is taken up by the resistant cancer cells. By inhibiting synthesis of the corresponding normal nucleosides with inhibitors to which the cancer cells are not resistant, incorporation of the toxic analogues into tumour DNA was enhanced. Although ^{125}IUdR is a convenient agent for exploring this approach and is highly cytotoxic when incorporated in DNA, the clinical potential of reverse role chemotherapy probably lies with the development of toxic non-radioactive nucleoside analogues.

The purpose of this study was to explore the possibility that drug resistance occurring at the cell level in cancers is a therapeutically exploitable characteristic.

There is a small range of human cancers that can usually be eradicated by conventional cytotoxic chemotherapy, whereas the generality of common epithelial cancers either fail to respond, or do so only for a limited time (Goldie & Goldman, 1984). The reasons for the limited range of clinically responding cancers remain to be identified. It was suggested (Bagshawe, 1986) that only certain cancers exhibit the high proliferation rate and high cell loss rate which were proposed as a necessary pre-requisite for eradication when the dosage of cytotoxic therapy is limited by effects on normal cell renewal populations. In the past 20 years clinical drug resistance has been increasingly associated with mechanisms operating at the cell level (DeVita, 1983; Curt et al, 1984).

It is common clinical experience that normal haemopoietic and gastro-intestinal mucosal tissues remain dose limiting and, apart from rare examples, do not exhibit increased resistance to cytotoxic action. Drug resistance is widely attributed to genetic instability in cancer cells (Nowell, 1976) with gene amplification demonstrated in some cases and with changes in target enzymes, nucleotide pools, multidrug resistance, P glycoprotein, topoisomerase I and II expression, glutathione transferase, drug inactivation, DNA repair and membrane transport etc. (Curt et al, 1984; Schimke, 1984; Kartner et al, 1985; Gross et al, 1986; Fox & Roberts, 1987).

Although it can be argued that resistance at the cell level is not proven as the primary cause of clinical resistance, there is ample evidence that resistance at the cell level does occur in at least some cases, whether it be the primary cause of clinical resistance or a secondary phenomenon resulting from exposure to cytotoxic agents. The question arises (Bagshawe, 1986) whether cell level resistance exhibited by cancer cell populations but not by normal cells provides a basis for discrimination against cancers. More specifically, if a cancer is resistant to a cytotoxic agent which inhibits DNA synthesis, then, during exposure of the patient or animal host to that agent, DNA synthesis would continue in the cancer cells while it would be arrested in normal cells. Under cover of the DNA synthesis inhibitor, administration of a potentially lethal nucleoside analogue would be expected to result in much greater incorporation of the analogue into cancer cell DNA than into normal cell DNA.

Such an approach would require that the arrest of DNA synthesis in normal cells be achieved for such a short period of time that significant cell loss would be avoided. It is also implicit that the biological life of the chosen nucleoside analogue be less than that same

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Address Requests for reprints to Professor K. D. Bagshawe, Cancer Research Campaign Laboratories, Department of Medical Oncology, Charing Cross and Westminster Medical School, London W6 8RP.

period of time so that it would be eliminated or degraded before normal cells re-engage in DNA synthesis.

In the present studies we used as the principal inhibitor of DNA synthesis hydroxyurea (HU), which acts by inhibiting ribonucleotide reductase (Krakoff et al, 1968). Limited studies were also performed with cytosine arabinoside (ara C) which probably acts by inhibiting DNA polymerase (Ho & Frei, 1971). Both drugs are used widely to arrest cells in S phase. Neither has a well established place in the treatment of solid human cancers, since clinical resistance is observed either *de novo* or is soon acquired.

^{125}I-5-iodo-2′-deoxyuridine (^{125}IUdR) was used both as an indicator of DNA synthesis and as a model for a lethal nucleoside. IUdR competes with thymidine for incorporation into DNA (Prusoff, 1959). IUdR incorporated into DNA may be retained for the life of the cell or transmitted to daughter cells. IUdR not incorporated into DNA undergoes cleavage to 5-iodo-5,6-dihydrouracil followed by rapid dehalogenation (Dethlefesen, 1970). Free ^{125}I is taken up by the thyroid gland or excreted in the urine. The reported biological plasma half-life is < 5 minutes in man (Klecker et al, 1985) and 7 minutes in mouse (Lee et al, 1986). Distribution determined by counting the radioactivity in tissues shortly after administration of ^{125}IUdR does not differentiate between ^{125}IUdR that is incorporated or not incorporated into DNA. Autoradiographic studies have therefore been used additionally to provide evidence of microanatomical distribution.

Since IUdR competes with thymidine for incorporation into DNA, the size of the thymidine pool, that is the amount of extracellular and intracellular thymidine, is critical to the percentage of IUdR incorporated into DNA (Knebbing & Werner, 1975). By administering drugs such as anti-folates and fluoropyrimidines which inhibit thymidine synthesis (Howell et al, 1981; Houghton et al, 1982) less intracellular thymidine is available to compete with administered IUdR so the percentage of administered IUdR incorporated into DNA may be increased (Hampton & Eidinoff, 1961; Kriss et al, 1962; Hofer, 1972; Benson et al, 1975). It is implicit in the approach that the cancer cells should not be resistant at the cell level to these inhibitors. It has also been reported that 5′-aminothymidine increases the uptake of IUdR into DNA (Fisher, 1986).

The object of the present study was therefore to determine whether a selective uptake of ^{125}IUdR into cancer cell DNA could be achieved in human xenograft models using combinations of various cytotoxic and other agents. Two critical indices were used in the assessment of each protocol and the potential for therapy is greatest when both indices are maximized. These were (I) the proportion of total administered dose retained per unit weight of tumour (per cent retention) and (II) tumour to normal tissue ratios. Small intestine and colon gave the higher ^{125}IUdR uptake values for normal tissues, and for uniformity we have used tumour to colon ratios.

Materials and methods

Normal male Balb/C, A2G and Nu/Nu mice (Balb derived) aged 6–8 weeks and weighing 20–27 g were supplied by our animal production unit and maintained with standard feed and water containing potassium iodide (0.1%) ad lib. Studies with the LS174/T tumour were performed on female Nu/Nu mice.

The CC3 tumour is a gestational choriocarcinoma from a hysterectomy specimen removed before the patient received any chemotherapy. It has been maintained as a xenograft in Nu/Nu mice since 1980 and produces human chorionic gonadotrophin. Established CC3 tumours have proved resistant to eradication by methotrexate, hydroxyurea, actinomycin D and etoposide. The MAWI tumour is a poorly differentiated mucoid adenocarcinoma of colon maintained both *in vitro* and in serial xenograft passage since 1982. The LS174/T is a moderately differentiated colonic adenocarcinoma kindly supplied by Dr G. Schlom, NCI, Bethesda, Maryland, USA. Tumour diameters at the start of experiments were in the range of 0.5–1.5 cm but, within each study, diameters were limited to the mean +20% and mice were distributed between control and study groups so as to minimize differences in tumour size.

Unlabelled IUdR was measured in plasma by high performance liquid chromatography using a sample preparation cartridge followed by injection on a Waters Bondapak (10 μ), and detection at 280 nm on a Waters Laudamax 480 LC spectrophotometer. Calibration curves were constructed using IUdR added to plasma and were linear in the range 0.5–5.0 μg/ml. Pharmacokinetic parameters were estimated using the interactive computer programme "Stripe" (Johnson & Woolard, 1983).

Blood samples were obtained by retro-orbital aspiration under anaesthetic and for clearance studies samples were obtained at intervals of 2, 5 and 10 minutes and then at 7-minute intervals up to 45 minutes.

Mice were sacrificed by neck dislocation 24 hours after injection of ^{125}IUdR, unless otherwise stated. The organs were removed immediately after death, blotted and then weighed. Before γ counting the tissues were digested in 7 M KOH for 12–18 hours and vortex mixed. Bone counts were determined by removing the ends of the right femur before weighing and digesting. Activity is expressed as counts/minute/gram of tissue. For histological examination and autoradiography, tissues were fixed in 10% buffered formalin for 24 hours. Bone was decalcified in an EDTA–formalin mixture (80 g EDTA in 950 ml distilled water plus 50 ml formalin) for 16 hours and then post-fixed in 10% buffered formalin for 8 hours. Tissues were processed through a graded alcohol sequence and an inhibisol/chloroform mixture to paraffin wax. Sections were cut at 4 μm and mounted on subbed slides (dipped in 0.5% gelatine in 0.05% potassium chromium sulphate in distilled water). Slides were covered by Kodak AR10 stripping film or a nuclear research emulsion K5 (Ilford)

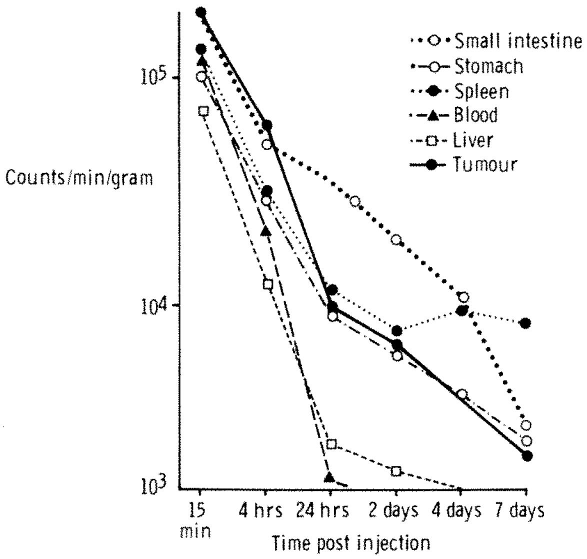

Figure 1. Six groups of four Nu/Nu mice bearing MAWI xenografts each received 4 μCi ^{125}IUdR (IV) and were sacrificed at intervals ranging from 15 minutes to 7 days later. The values show the rates of fall of radioactivity in some normal tissues and tumour.

and autoradiographs prepared by standard methods. Nuclear grain counts made on autoradiographs prepared using K5 emulsion were performed as previously described (Bagshawe et al, 1987) and cumulative frequency ogives were constructed for both the CC3 tumour and normal mouse colon.

Hydroxyurea was provided in powder form by Squibb & Sons Ltd, and was dissolved in a sterile acid phosphate buffer (pH 5.95). Methotrexate (Lederle), cytosine arabinoside (Upjohn), 5-fluorouracil (5-FU) (Roche) were made up in sterile normal saline, 5-iodo-2′-deoxyuridine was obtained from BDH Chemicals, Ltd, Poole, Dorset, UK; 5-fluoro-2′-deoxyuridine and 5′-amino thymidine were obtained from Sigma Chemical Co., Poole, Dorset, UK. [^{125}iodo]5-iodo-2′-deoxyuridine (5 mCi/μg) was obtained from Amersham International, Amersham, Bucks, UK.

Results

Following intraperitoneal (IP) injection of 1 mg IUdR in 0.8 ml normal saline into Nu/Nu mice a $t_{1/2}$ absorption of 2 minutes was obtained with an elimination $t_{1/2}$ of 11.5 minutes. Area under curve (AUC) was 14.73 μgh l^{-1} and total clearance 11.13 ml/minute with a distribution volume of 0.026 l. For 1 mg IUdR given intravenously (IV) the $t_{1/2}$ was 6 minutes, $t_{1/2}\,\alpha$ 3.42 minutes and $t_{1/2}\,\beta$ 10.4 minutes with AUC 20–38 μgh l^{-1}, total clearance 0.80 ml/minute and distribution volume 0.012 l.

When 10 μCi ^{125}IUdR was given (IV) to Nu/Nu mice xenografted with the MAWI tumour the high radioactivity values found in some tissues initially started to fall rapidly. Serum and liver values continued to fall reaching low values by 24 hours whereas gastro-intestinal tract and spleen values were still elevated at 7 days (Fig. 1).

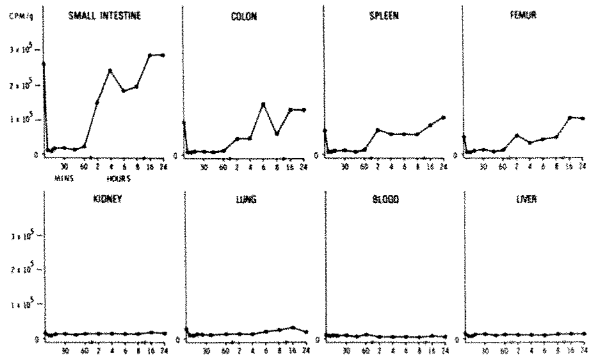

Figure 2. Hydroxyurea was given 50 mg/kg (IP) followed at 5, 10 and 15 minutes and the other intervals shown by 10 μCi ^{125}IUdR (IV) to Balb/C mice, four per group. The mice were sacrificed at 24 hours and the organs counted.

We determined the time interval between administration of HU and inhibition of ^{125}IUdR uptake in the cell renewal populations of normal A2G mice. The results (Fig. 2) indicated that ^{125}IUdR values in high uptake normal tissues were sharply suppressed within 5 minutes of HU administration. Values for all tissues remained low through the first 60 minutes but those for cell renewal tissues were increasing by 2 hours. Values for stomach (not shown in Fig. 2) tended to be variable and may not reflect uptake into DNA since high tissue counts were not reflected in correspondingly high nuclear grain counts; skin counts also varied greatly owing to contamination with urine and high counts were not reflected in high nuclear grain counts.

The effect of different doses of HU and ara C on uptake of ^{125}IUdR by CC3 tumour and normal cell renewal tissues was studied. The results of tissue counting are shown for colon and tumour for each group in Fig. 3. The marked susceptibility of normal renewal tissues to HU contrasts with the relatively small variation in uptake by tumour tissue indicating resistance of the CC3 tumour to HU. It was also noted that at doses of 50 and 100 mg/kg, HU alone gave positive tumour to colon ratios. At all dose levels of ara C tested there was marked reduction in ^{125}IUdR uptake by the CC3 tumour.

The object of the next study was to determine whether there was interaction between the dose of HU used to arrest DNA synthesis and that of an inhibitor of thymidylate synthesis. The results are shown in Table I. The higher of two dose levels of HU produced the more favourable tumour to colon ratios, whereas the higher doses of 5-FU were associated with a higher percentage of ^{125}IUdR retained in the tumour. It was concluded that the effects of different dosages of these two agents do not function in this model as independent variables.

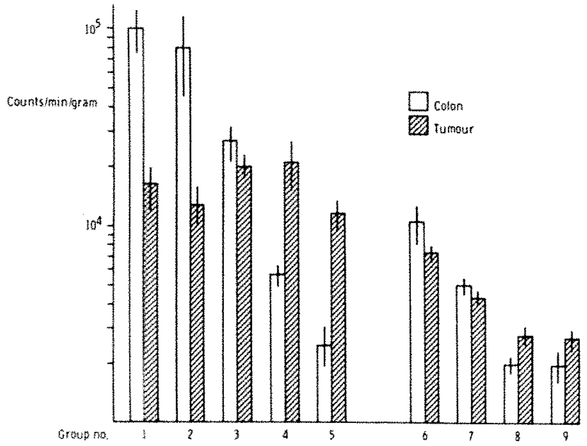

Figure 3. The effect of HU and ara C on uptake of ^{125}IUdR by colon and CC3 tumour. Four groups each of four Nu/Nu mice bearing CC3 xenografts received HU (IP) and four groups received ara C 15 minutes before 10 μCi ^{125}IUdR (IV). Group 1: saline; Group 2: 12.5 mg/kg HU; Group 3: 25 mg/kg Hu; Group 4: 50 mg/kg HU; Group 5: 100 mg/kg HU; Group 6: 1 mg/kg ara C; Group 7: 4 mg/kg ara C; Group 8: 20 mg/kg ara C, Group 9: 100 mg/kg ara C. The mice were sacrificed at 24 hours.

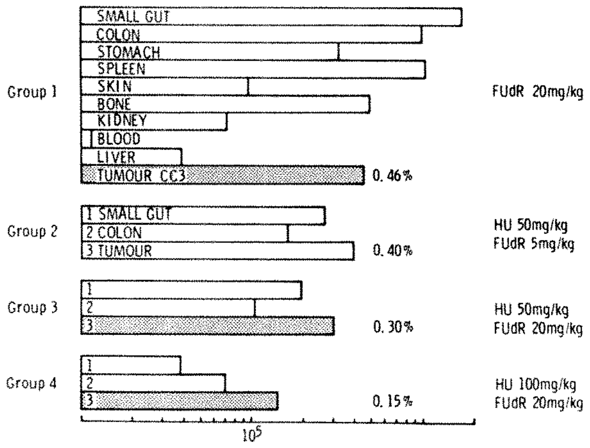

Figure 4. The effect of dose combinations of FUdR and hydroxyurea on CC3 tumour/normal tissue ratios. Group 1 received 20 mg/kg FUdR (IP) 15 minutes before 5 μCi ^{125}IUdR (IV). Group 2 received HU 50 mg/kg (IP) followed after 15 minutes by FUdR 5 mg/kg (IP) and after a further 15 minutes by 5 μCi ^{125}IUdR (IV). Groups 3 and 4 differed from Group 2 only by the dosages shown. The percentage of total ^{125}IUdR administered retained per gram of tumour is indicated for each group.

We determined tumour to colon ratios and percentage of administered ^{125}IUdR retained by tumour in the presence of HU when 5-fluoro-2′-deoxyuridine (FUdR) replaced 5-FU as an inhibitor of thymidine synthesis (Fig. 4). Over the range of dose combinations used, HU with FUdR was inferior to the most favourable dose combination for HU and 5-FU.

The effect of 5′-aminothymidine (5′AT) was examined. When 5′AT was given after normal saline there was a reduction in uptake of ^{125}IUdR by normal tissues (Fig. 5). When 5′AT was given after HU and before ^{125}IUdR the tumour to colon ratio was less favourable than with HU alone. There was no significant difference between IP and IV routes for 5′AT. Increasing the dose of 5′AT to 450 μg did not improve the ratio.

In order to determine whether the capacity to take up ^{125}IUdR was readily saturated we also tested the effect of unlabelled IUdR (IP) on uptake of ^{125}IUdR (IV) over a concentration range unlabelled IUdR:^{125}IUdR of 1000–25 000 : 1. At the highest dose level the amount of ^{125}IUdR in tumour tissue was reduced but the tumour : colon ratio was enhanced at all dose levels (Table II).

Tumour to normal ratios were studied with increasing doses of ^{125}IUdR given as a single IP injection over a 100-fold range. The higher the dose the greater was the amount taken up (Fig. 6). The percentage of total injected dose retained by tumour fell as the dose increased and at the highest dose level was 40% of that

Table I. The effect of different dose combinations of HU and 5-FU on tumour to colon ratio and percentage of total dose of ^{125}IUdR retained per gram of CC3 tumour

HU (mg/kg)	5-FU (mg/kg)	Tumour : colon ratio	Percentage retained per gram of tumour
50	5	1.3	0.27
100	5	3.9	0.05
50	20	2.7	0.30
100	20	4.6	0.35
50	40	1.4	0.51
100	40	5.7	0.13
—	40	0.4	0.49
50	—	3.7	0.12
100	—	4.7	0.07
—	—	0.16	0.09

Table II. Effect of simultaneously administered unlabelled IUdR (IP) on ratio tumour : normal tissue for uptake of ^{125}IUdR (1 ng)

	Dose of cold IUdR			
	0	1 μg	5 μg	25 μg
Small gut	2.5	4.8	3.6	4.6
Colon	3.2	9.0	5.0	4.4
Blood	24.0	33.7	22.0	14.0
Liver	16.4	22.3	16.7	11.6
Percentage of injected dose ^{125}IUdR per gram of tumour	0.25	0.30	0.24	0.15

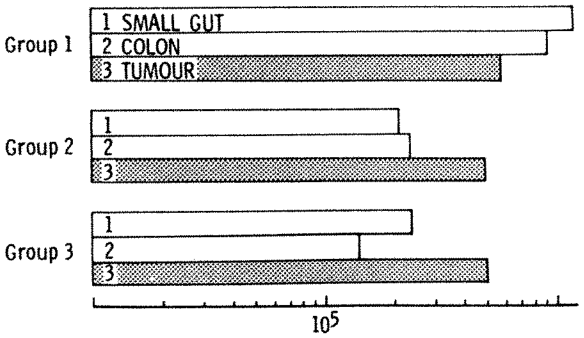

Figure 5. The effect of 5′AT on tissue distribution of ^{125}IUdR in CC3 bearing Nu/Nu mice. Group 1 received N/saline (IP) at time zero, 5′AT 200 μg (IV) 15 minutes later and ^{125}IUdR 2.5 μCi (IV) after a further 5 minutes. Group 2 received hydroxyurea 50 mg/kg (IP) at time zero, 5′AT 200 G μg (IV) 15 minutes later and ^{125}IUdR 2.5 μCi (IV). Group 3 protocol was identical to Group 2 except that the 5′AT was given IP.

at the lowest dose level. Tumour to colon ratios also tended to fall at the higher dose levels as determined by tissue counts at 24 hours.

Five groups of four mice each bearing LS174/T tumour were treated with similar protocols. Groups were killed and tissue counted at intervals over a period of 7 days (Fig. 7). The ratio of area under the curve for tumour/small intestine, for the 7-day period was calculated to be 3.08. Taking the period for 24 hours to 7 days, the ratio was 13.6 reflecting the clearance of free ^{125}I in the first 24 hours.

Tumour uptake and tumour to highest normal tissue ratios at 24 hours were determined for CC3 and LS174/T on the basis of previous studies (Fig. 8). With the CC3 tumour 0.68% of the administered dose was retained at 24 hours with a tumour to small intestine ratio of 9.8 and a tumour to colon ratio of 14 by tissue counting 24 hours after 5-FU 20 mg/kg, IUdR 1 μg, HU 100 mg/kg IP followed 5 minutes later by ^{125}IUdR 50 μCi IV. LS174/T tumour to small intestine and colon ratios of 11.5 and 34.3, respectively, were obtained and 1.09% of administered dose was retained at 24 hours after methotrexate (MTX) 5 mg/kg and IUdR 5 μg IP, followed by HU 50 mg/kg IP 30 minutes later and ^{125}IUdR 10 μCi IV after a further 5 minutes.

Autoradiography of CC3 tumours was performed in an experiment which gave a tumour to colon ratio of 13.8

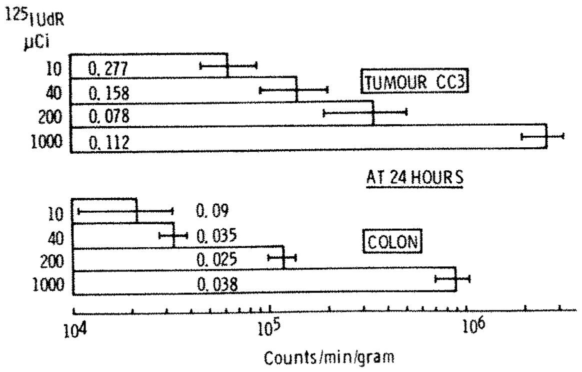

Figure 6. CC3 tumour and colon counts 24 hours after different amounts of ^{125}IUdR. Each group of five mice received HU 50 mg/kg, MTX 5 mg/kg and ^{125}IUdR (IP). Group 1 received 10 μCi; Group 2: 40 μCi; Group 3: 200 μCi and Group 4: 1000 μCi. The percentage of total ^{125}IUdR given and retained per gram of tumour or colon is indicated.

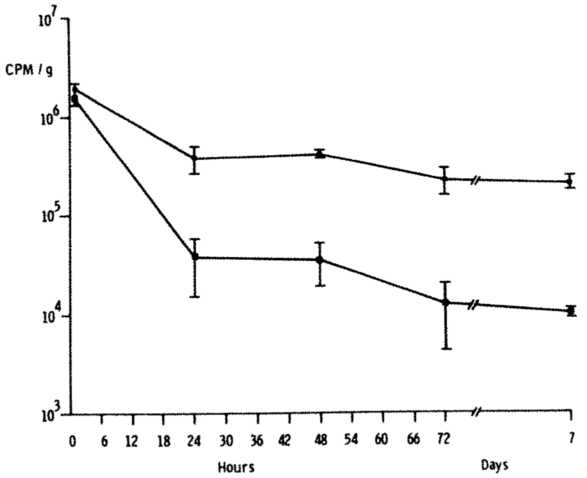

Figure 7. Five groups each of four Nu/Nu mice bearing LS174/T tumours received 5-FU 15 mg/kg and IUdR 0.2 μg (IP) 30 minutes before 5-FU 20 mg/kg and HU 100 mg/kg (IP) followed after 5 minutes by 50 μCi ^{125}IUdR (IV). The mice were killed at the times indicated and the tissues counted. Upper curve is tumour radioactivity, lower curve is small intestine.

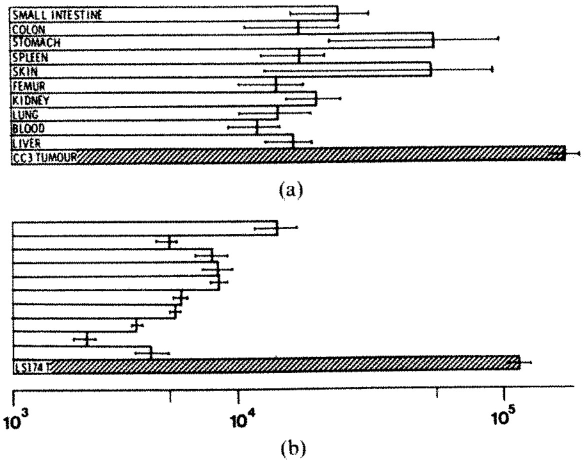

Figure 8. (a) CC3 tumour bearing mice received (IP) HU 100 mg/kg, 5-FU 20 mg/kg and IUdR 1 μg. Five minutes later 50 μCi ^{125}IUdR was given (IV). The mice were killed and tissues counted 24 hours later. (b) LS174/T tumour bearing mice received (IP) MTX 5 mg/kg and IUdR 5 μg; 30 minutes later 50 mg/kg HU was given (IP) followed by 10 μCi ^{125}IUdR (IV) 5 minutes later. Tissue counts shown at 24 hours.

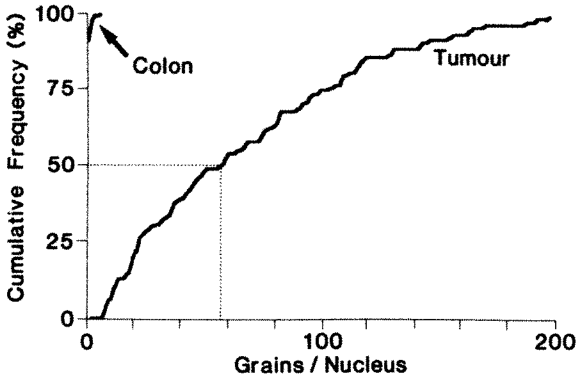

Figure 9. Cumulative frequency ogives for CC3 tumour and colon 24 hours after ^{125}IUdR. The mice received HU 100 mg/kg, 5-FU 20 mg/kg (IP) at time zero and repeated 60 minutes later; 100 μCi and 400 μCi ^{125}IUdR were given (IV) 5 minutes after the first and second doses of HU and 5-FU, respectively.

at 24 hours by tissue counting. The corresponding tumour to colon ratio by nuclear grain counting was 150:1. Cumulative frequency ogives for tumour and colon at 24 hours are shown in Fig. 9. Fifty per cent of tumour nuclei contained > 57 grains and there were no unlabelled cells. In the colon, 90% of nuclei were unlabelled and none contained more than 8 grains.

Discussion

The data presented here indicate that in our models an inhibitor of DNA synthesis can be used to achieve a highly selective retention of a nucleotide analogue in tumour cell nuclei.

We have confirmed earlier observations in rodents that ^{125}IUdR is retained in tissues associated with a high cell turnover such as intestine, spleen and tumour suggesting that ^{125}IUdR is incorporated into newly synthesized DNA (Hampton & Eidinoff, 1961; Kriss et al, 1962). Loss of epithelial cells into the intestinal lumen would account for the decline in intestinal activity over 7 days and lethal doses of ^{125}I would increase the rate of cell loss. ^{125}IUdR not incorporated into DNA was rapidly metabolized and 80–90% of the radioactivity was excreted within 24 hours.

By giving HU to normal mice we showed that uptake of ^{125}IUdR by intestine, spleen and bone marrow was maximally suppressed within 5 minutes. The duration of suppression by a 50 mg/kg dose of HU was not less than 1 hour for any normal tissue but by 2 hours normal cell renewal tissues resumed uptake. This suppression of uptake in normal tissues contrasted with uptake of ^{125}IUdR by CC3 tumour which remained close to control levels when doses up to 100 mg/kg of HU were given. Also the higher doses of HU gave positive tumour to intestine uptake ratios. Thus there was a clear difference in the effect of HU on ^{125}IUdR uptake by normal tissue and this tumour. Broadly similar results were obtained with LS174/T tumours although this tumour was not completely resistant and HU depressed ^{125}IUdR uptake.

Within the range of dose combinations employed, 5-FU and MTX proved effective at increasing tumour uptake of ^{125}IUdR, both in terms of tumour to intestine ratio and in the percentage of administered dose retained in the tumour but only when co-administered with HU. However, the results indicate that HU and 5-FU interact. The higher the dose of 5-FU used the higher the dose of HU required to achieve a satisfactory tumour:intestine ratio. This is consistent with the observation of Elford et al (1977) that agents which block thymidylate synthesis lower intracellular pools of deoxythymidine 5′ phosphate and thereby increase ribonucleotide reductase activity. However, we have not determined the mechanism by which 5-FU increases ^{125}IUdR uptake. It is relevant that neither 5-FU nor MTX produce marked growth delay with the CC3 and LS174/T tumours so that this "clinical resistance" is not reflected in resistance at the cell level in so far as increased uptake of ^{125}IUdR indicates interference with thymidine synthesis. Cell level resistance to inhibitors of thymidine synthesis would presumably preclude their use in this approach.

In one experiment with FUdR, the percentage uptake of ^{125}IUdR was comparable to that obtained with 5-FU but the tumour to colon ratio was less favourable. Although pre-treatment with 5′-aminothymidine altered tumour to colon ratios favourably when used as a single agent, in our *in vivo* studies with HU the ratios were less favourable than with HU and ^{125}IUdR alone. It might be expected that any amount of cold IUdR would reduce the uptake of ^{125}IUdR by the tumour. However, this occurred only to a limited extent and at the highest dose levels so that a high capacity to incorporate IUdR into tumour DNA existed.

Evidence that increasing doses of ^{125}IUdR are associated with increased uptake by normal tissue as well as tumour was obtained over a 100-fold range of bolus injections. Although the percentage tumour retention of ^{125}IUdR at the highest dose (1000 μCi) was reduced compared with the lowest dose (10 μCi), these data also suggest that uptake mechanisms were not saturated even at the highest dose levels tested. The possibility that delayed clearance of ^{125}I not bound to DNA contributed a greater proportion of the tissue counts at the higher dose levels has not been excluded.

Tumour to intestine ratios of the order of 15:1 were obtained both with the CC3 and LS174/T tumours with percentage retention of administered dose in the range of 0.25–1.5 with single doses of ^{125}IUdR. This compares well with ratios attained previously after 3- or 5-day sequential therapy (Bagshawe et al, 1987), but it is unlikely that we have yet optimized tumour uptake or tumour to normal tissue ratios. We have previously reported that autoradiographs of tumour and normal tissues obtained after treatment of mice with various protocols show nuclear grain count ratios for tumour to intestine that are 5–15 times more favourable than tissue count ratios. This is illustrated in the present studies with corresponding tissue count ratios and nuclear grain count ratios for tumour : colon of 13.8 and 150, respectively. Cumulative frequency ogives confirm that, while a high proportion of the tumour cell nuclei contain relatively large numbers of grains, very few nuclei in the intestinal crypts accumulated grains when HU was used to inhibit DNA synthesis.

The "areas under the curve" reported here by tissue counting, and the further enhancement shown by nuclear autoradiographs, indicate that tumour to highest normal tissue ratios of the order of 100 : 1 may be obtained following a single administration of the nucleoside with HU and an inhibitor of thymidine synthesis.

Although we have used uptake of ^{125}IUdR as a marker of nucleoside incorporation, the question of the most suitable nucleoside(s) for therapeutic purposes needs consideration. ^{125}IUdR has long been known to have a powerful cytotoxic action when incorporated in DNA (Hofer & Hughes, 1971) through disintegration of ^{125}IUdR by electron capture and Auger cascade emission which results in non-repairable double strand breaks (Burki et al, 1973). The energy of disintegration was absorbed within 25 nm so that when ^{125}I was located on the cell membrane its cytotoxicity was less than a hundredth that for the ^{125}IUdR incorporated into DNA (Hofer et al, 1981). It was estimated that the mean lethal dose for Chinese hamster ovary cells was 100 disintegrations of ^{125}IUdR in DNA and that 500 disintegrations produced a 99% kill. Thus to accumulate 500 disintegrations during an arbitrary period of 100 hours in each daughter of an S phase cell would require the incorporation of 2.25×10^4 molecules of IUdR into the DNA of an S phase cell assuming a specific activity of 5 mCi/μg ^{125}IUdR and that the cell proceeds through the subsequent mitosis successfully. For comparison, in a human cell with an S phase of 10 hours' duration, about 2.3×10^4 thymidine molecules are incorporated per second. Evidence for marked variation in susceptibility of cells *in vitro* to ^{125}IUdR has however been presented (Schumacher et al, 1974).

Earlier attempts to modify the *in vivo* distribution of IUdR with MTX (Hampton & Eidinoff, 1961) and fluoropyridines (Kriss et al, 1962) resulted in increased uptake by all mitotically active tissues. The use of HU to synchronize proliferative cell populations and improve scintigraphic localization of tumours with ^{131}IUdR was explored by Schumacher et al (1974). The detection of lung tumours in rats was enhanced, but the approach does not appear to have been followed up and the timing of HU and ^{125}IUdR administration differed from that used in the present studies.

The question whether lethal amounts of ^{125}IUdR would be taken up by a sufficiently high proportion of tumour cells to achieve a therapeutic effect remains open. Since uptake of ^{125}IUdR is largely restricted to S phase cells, it would be anticipated that tumours with a high labelling index would be the more susceptible. However, long intermitotic times allow labelled cells longer to accumulate a lethal dose before the ^{125}IUdR is distributed into daughter cells. In any case, multiple treatments would be necessary to ensure uptake into all clonogenic cancer cells. Although IUdR, like other nucleosides, has a short biological half-life, the 60-day radio-half-life of ^{125}I is a serious disadvantage since cold iodine loading does not completely inhibit thyroid uptake and gastric secretion of ^{125}I. Moreover it would present substantial problems in radioactive waste disposal.

Limitation of the toxicity of ^{125}IUdR to cells in S phase at the time of administration could be a serious impediment to its effectiveness particularly in tumours with a low labelling index, and is comparable to the similar limitation of cell cycle specific cytotoxic drugs. Alternative radionuclides with a wider range of action that might be incorporated into a nucleoside analogue include the halogen astatine-211 an α-particle emitter with a half-life of 7.2 hours. This has the potential to kill cells over a distance of 4–8 cell diameters. It would undoubtedly be valuable when located in tumours but normal tissues including thyroid would also be affected and secretion of the halogen via stomach and kidneys and its short half-life could be serious limitations (Cobb et al, 1988). Moreover, calculations indicate that the amount of astatine that would need to be administered to a patient assuming that 1% of the dose is taken up per gram of tumour, would be in the order of several hundred millicuries.

The general feasibility of the approach therefore appears to rest on non-radioactive nucleoside analogues. In non-radioactive form IUdR and the bromine analogue (BUdR) are not sufficiently toxic to be useful but other nucleoside analogues capable of incorporation into DNA may have greater potential. 2-bromo-2′-deoxyadenosine has been found to be active against L1210 lymphocytic leukaemia in mice (Carson et al, 1980) and human melanoma cell lines (Parsons et al, 1986) following incorporation into DNA and inhibition of DNA synthesis. Arabinosyl-5-azacytosine has entered clinical trials (Grem et al, 1987). Phosphonomethyl ethers of acyclic nucleoside derivatives have also shown activity in murine tumour models (Rose et al, 1990). The damage to the cancer cells resulting from incorporation of the nucleoside analogue would clearly need to exceed damage to the normal renewals tissues resulting from the temporary inhibition of DNA synthesis.

The present study indicates that, in mice with xenografts of human cancers showing cell level resistance to an inhibitor of DNA synthesis such as HU, administration of that inhibitor together with other relevant antimetabolites can achieve a highly selective incorporation of a nucleoside analogue. This may act as a stimulus to the development of other toxic nucleoside analogues.

Acknowledgments

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Tissue dose estimates following the selective uptake of ^{125}IUdR and other radiolabelled thymidine precursors in resistant tumours

By *J. L. Humm, PhD, K. D. Bagshawe, MD, S. K. Sharma, MSc and G. Boxer, BSc

Cancer Research Campaign Laboratories, Department of Medical Oncology, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, UK

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Abstract. For the purposes of evaluation of the therapeutic potential of the radiohalogenated thymidine analogue ^{125}IUdR, estimation of the radiation dose to the tumour cells and normal tissues is important. To determine the dose to any tissue from the radionuclide ^{125}I is not simple, since the major emissions are very short-range Auger electrons. The cytotoxicity of ^{125}I is strongly dependent on the position of the decay relative to the DNA, the principal target for cell sterilization. Estimates of the cytotoxicity of ^{125}I based on the traditional MIRD recommended formulation (ICRU Report 32, 1979) may produce gross underestimates if it is incorporated into the DNA via the thymidine precursor ^{125}IUdR. In this work, tissue count and autoradiography (ARG) data from studies by Bagshawe et al were used to estimate tissue doses following the administration of ^{125}IUdR to LS174/T (a colorectal carcinoma) and CC3 (a choriocarcinoma) tumour-bearing animals, after a hydroxyurea block of the normal tissue turnover. The tumour cell toxicity is estimated from ARG data on the degree of ^{125}I incorporation into the cell nucleus. Major drawbacks with ^{125}I for this type of therapy are the long 60-day half-life, leading to radiological and waste disposal problems and the extreme short range of the radiotoxic effects. Possible alternative radiohalogens, ^{123}I, ^{77}Br, ^{131}I and ^{211}At, are suggested in place of ^{125}I in the thymidine analog iododeoxyuridine. Dose calculations are performed and cytotoxicities estimated on the assumption that their biological retention characteristics are the same as for ^{125}IUdR.

For a long period, the high radiotoxicity of Iodine-125 (^{125}I) incorporated into the DNA as the thymidine analog 5 iodo-2′-deoxyuridine-125 (^{125}IUdR) remained an enigma in radiobiology. Hofer (1980) and Kassis et al (1988) had shown by cell survival assays that DNA incorporated ^{125}IUdR exhibited a high LET radiotoxicity similar to α-particle irradiation. However, experiments with ^{125}I-concanavalin A, a cell membrane affinic lectin (Hofer, 1980), and ^{125}I-iodoantipyrine (Commerford et al, 1980), a non-DNA binding agent which diffuses freely through cells, demonstrated survival curves similar to those following X and γ irradiation.

The high yield of DNA double strand breaks (dsb) associated with the decay of ^{125}I incorporated into the DNA, about one dsb per decay (Krisch et al, 1977; Tisljar-Lentulis et al, 1987) can be explained by the large energy deposition in the DNA by the prolific Auger electron emission (Charlton & Humm, 1988). There is now sufficient evidence that other electron capture and internal conversion decaying radionuclides are extremely effective in producing DNA dsbs. It is generally postulated that the magnitude of the DNA damage will depend on the magnitude of the Auger cascade, which in turn depends upon the atomic number Z of the element and the number of electron capture and/or internal conversion events per disintegration, *i.e.* on the radionuclide decay scheme (Sastry et al, 1988; Humm & Charlton, 1989). Table I shows the fraction of electron capture and internal conversion events per decay for the radionuclides discussed in this paper. For a detailed discussion of the calculations of the Auger spectra for ^{125}I and ^{123}I the reader is referred to Charlton and Booz (1981) and Humm et al (1981).

Method

Estimation of tissue doses from ^{125}IUdR

Tissue dose estimates were performed using the data from our previous paper (Bagshawe et al, 1991) in which LS174/T-bearing nu/nu mice were administered 1.85 MBq (50 μCi) of ^{125}IUdR. These mice had received prior treatment with 15 mg/kg 5-fluorouracil (5-FU) and

Table I. Yield of electron capture (EC) and internal conversion (IC) events for the radiohalogens discussed in the text of ICRP Report 38 (1983). The sum of the fraction of EC and IC gives the fraction of Auger cascades per disintegration

Isotope	Half-life	Number per decay	
		Electron capture	Internal conversion
Iodine-125	60 days	1.0	0.93
Iodine-123	13.2 hours	1.0	0.16
Bromine-77	56 hours	1.0	0.01
Iodine-131	8.04 days	0.0	0.06
Astatine-211	7.2 hours	0.58	0.0

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* Present address: Joint Center for Radiation Therapy, Harvard Medical School, 50 Binney Street, Boston, MA 02115, USA.

Table II. Radiation doses (Gy) calculated using the MIRD formulation, based on retention curves for ^{125}IUdR in LS174/T-bearing nu/nu mice fitted to five serial activity time points: 1 hour, 24 hours, 48 hours, 72 hours and 7 days. Twenty mice were used in this study (four per time point) and each was given 1.85 MBq of ^{125}IUdR following administration of cold IUdR, 5-FU and HU (as described in text). Assuming no change in the retention curve from ^{125}IUdR, resulting from the chemistry of labelling with alternative halogen radionuclides, ^{123}I, ^{131}I and ^{211}At, the radiation dose following a 1.85 MBq injection of these respective halogenated thymidine precursors, under identical conditions, was evaluated. Experimental evidence shows a linear tumour incorporation of ^{125}IUdR with injected activity at least up to 37 MBq. Therefore, the tissue doses can be assumed to scale up linearly for the iodine isotopes and possibly other halogen isotopes until this activity is reached

	^{125}I	^{123}I	^{131}I	^{211}At
Half-life	60 days	13.2 hours	8 days	7.2 hours
Blood	0.0026	0.0033	0.024	0.75
Tumour	0.0192	0.0032	0.112	0.53
Tumour (0–100 hours)	0.0078	0.0032	0.065	0.53
Liver	0.0011	0.0008	0.009	0.15
Kidney	0.0029	0.0017	0.019	0.32
Lung	0.0041	0.0012	0.014	0.25
Spleen	0.0019	0.0009	0.011	0.17
Colon	0.0016	0.0009	0.011	0.17
Skin	0.0060	0.0014	0.023	0.31
Stomach	0.0036	0.0023	0.025	1.03
Small intestine	0.0018	0.0013	0.033	0.28
Bone	0.0018	0.0012	0.014	0.24

0.2 μg cold IUdR (35 minutes before) and 100 mg/kg hydroxyurea (HU) and 20 mg/kg 5-FU (5 minutes before) given intraperitoneally (IP) to inhibit DNA synthesis selectively, and thus ^{125}IUdR incorporation, in non-tumour tissues. Tumours that exhibit resistance to HU are not blocked, continue to cycle, and thus readily incorporate the radioactive thymidine precursor. The count rate data for each of the following tissues were fitted with a single or dual exponential equation: blood, tumour, liver, kidney, lung, spleen, colon, skin, stomach, small intestine and bone. Each curve was integrated to obtain the cumulative activity. The radiation dose was then calculated by the standard MIRD procedure (Burki et al, 1973) from the product of the cumulative activity and the equilibrium dose constant for the non-penetrating (electron) component of the radionuclide emission. The penetrating γ- and X-ray emission components were assumed to have an absorbed fraction of zero which for mice is a good assumption. For man, estimates of the photon dose to the dose limiting tissues would need to be made. The calculated tissue doses are given in Table II.

The radiation doses to all tissues for this injected activity are extremely small and reflect the rapid clearance of ^{125}IUdR from the blood pool. The tissue toxicity from ^{125}I not incorporated into the DNA at this administered activity (1.85 MBq) is negligible. However, the problem of estimating tissue radiotoxicity is not a simple one, since the toxicity may not be proportional to the cumulative source activity in the tissue of interest. The reason for this is the very marked variation of Auger source toxicity between DNA incorporated and non-incorporated material (Hofer, 1980; Charlton, 1986). The efficacy of ^{125}IUdR incorporated in the cell's DNA for 99% cell sterilization has been variously estimated to lie between 200 and 500 disintegrations per cell depending on the cell line (Burki et al, 1973; Hofer, 1980; Liber et al, 1983). Therefore, any attempt to estimate radiotoxicity must include the fraction of DNA incorporated radionuclide in the respective tissue.

Intranuclear uptake of the radiolabel

Studies of the loss of tissue activity in histological processing and autoradiography both demonstrate a significantly greater fraction of intranuclear source material in tumour compared with other tissues. In the histological processing of the colon, it was found that up to 82% of the activity could be lost in the stages of formalin fixation and alcohol displacement of the fixative. This suggests that most of the ^{125}IUdR was in the unbound form. For the tumour the activity losses were low, between 8% and 16%, suggesting a high level of incorporation into the DNA. This is corroborated by analysing autoradiographs of the tumour which show that over 90% of the grains produced by ^{125}I decays overlap with tumour cell nuclei. For the colon the grain density is much lower, owing to processing losses, and very few grains are associated with ^{125}I decays in the nuclei (see Fig. 9, Bagshawe et al, 1991, for tumour and colon cumulative grain frequency plots following an administration of 3.7 MBq (100 μCi) of ^{125}IUdR followed by a further 14.8 MBq (400 μCi) 1 hour later after prior blocking with HU).

If it is assumed for the non-tumour tissues that the level of ^{125}IUdR incorporation into the DNA is negligible, as the autoradiographs suggest, then the normal tissue toxicity from the emitted radiation will result from the longer range low LET effects associated with the Auger and internal conversion electrons. For the tumour, the ^{125}IUdR is predominantly intra-nuclear and probably DNA bound. If this is true, the maximal tissue toxicity can be estimated. The cumulative specific activity of ^{125}I in the tumour, obtained from the tissue counts, when expressed in units of Bq.s is equal to the number of disintegrations in the tumour. The cumulative specific activity integrated over all time is 5.884×10^9 Bq.s/g. The tumour clearance is governed by two components: a short half-life component of ~1 hour, possibly because of halogenation, and a longer half-life component of ~7 days. From the combined effect of these two half-lives, 40% of the ^{125}I disintegrations in the tumour occur within 100 hours. Depending on the tumour cell density, the number of disintegrations per cell can be calculated, *e.g.* for 10^8 cells/g this would result in ~24 decays/cell. A uniform labelling of cells is unlikely. Some cells probably receive much higher levels of the isotope than this average, whilst non-cycling cells in G_0 take up none. Results of Liber et al (1983) have shown 50% cell inactivation in a human lymphoblast cell line, with as low as 27 disintegrations per cell. This potential toxicity to the tumour produced by the very short range Auger emission component, which is effective when the source is bound to the DNA, is considerably greater than that suggested by MIRD dose estimates. Because the high Auger toxicity phenomenon is of such short range, only affecting the cell incorporating the radiolabel, a major difficulty with this proposed therapy is the heterogeneity of ^{125}IUdR uptake. The heterogeneity of ^{125}IUdR incorporation is the result of the asynchrony of the tumour cell population (only cells within or entering the S phase incorporate the precursor), and variations of incorporation rate as the cell transits S phase resulting in a differential vulnerability of cells in different stages of S phase. This problem is also aggravated by the long 60-day half-life of ^{125}I.

Results and discussion

Dosimetry of alternative Auger emitting radiohalogens as thymidine analogs

In order to obtain 500 disintegrations of ^{125}I within a cell cycle time of 100 hours, one would require the incorporation of ~10 500 ^{125}IUdR molecules per cell genome. This much larger number of radiolabels is necessary to ensure the required number of disintegrations within the specified 100-hour cell cycle time. If the cell cycle time were only 10 hours, then approximately 10 times, *e.g.* 105 000, the number of ^{125}IUdR molecules would be required per cell genome to result in the same toxocity prior to cell division, and dilution of activity in the cell progeny. This redundant excess with ^{125}I may be overcome by using alternative Auger emitters, *e.g.* ^{123}I (half-life = 13.2 hours) or ^{77}Br (half-life = 56 hours). Because of the short half-life of ^{123}I more than 99% of the incorporated isotope will have decayed within 100 hours. Initial double strand break yields for ^{123}I and Bromine-77 (^{77}Br) have recently been estimated by Humm and Charlton (1989) relative to ^{125}I per decay to be 0.66 and 0.35, respectively. If cell survival is linearly related to double strand break yield, then 500/0.66 and 500/0.35 decays of these respective radionuclides are required for 99% cell sterilization.

Based on the same mice pharmacokinetic data used to calculate the tissue doses for a 1.85 MBq administration of ^{125}IUdR, doses were recalculated replacing ^{125}IUdR with the same activity of ^{123}IUdR. It was assumed that the isotopic substitution of ^{123}I for ^{125}I does not affect the biological retention characteristics of the thymidine precursor in any of the tissues. The results are shown adjacent to those for ^{125}IUdR in Table II. They illustrate the lower tissue doses, including tumour, per unit administered activity of ^{123}IUdR than with ^{125}IUdR. This is because of the much shorter half-life and consequently fewer disintegrations per unit activity. Once again, these tissue doses from ^{123}I are so low that tissue radiotoxicity is negligible. The number of ^{123}I disintegrations in the tumour tissue per gram corresponding to the calculated tumour dose is 7.05×10^8, and the double strand break induction from specific incorporation of ^{123}I into the DNA will again be the dominant mechanism of cell killing. A disadvantage of the shorter lived isotope is the poorer tumour/normal tissue dose ratios. The effective gain in using ^{123}I, therefore, hinges on the fraction of ^{123}IUdR incorporation into the DNA of the tumour relative to the dose limiting tissues. If the uptake of ^{123}IUdR in the dose limiting tissues is low, as previously suggested, then there may be some benefit to using ^{123}I in place of ^{125}I. The smaller number of ^{123}IUdR molecules requiring incorporation may in part assist in overcoming the problem associated with cellular uptake heterogeneity. However, at the activities anticipated, the radiation cytotoxicity due to "cross-fire" would be insubstantial and therefore proposed therapies with either of these isotopes, or with ^{77}Br, rely on the sufficient incorporation of the radiolabelled thymidine precursor in every clonogenic tumour cell.

Dose escalation studies with up to 3.7×10^7 Bq (1 mCi) of ^{125}IUdR in CC3 and 7.4×10^6 Bq (200 μCi) with LS174/T tumour-bearing mice show an almost linear tumour uptake (at 24 hours time point) of ^{125}IUdR with administered activity, demonstrating that at these levels of ^{125}IUdR there is still no saturation in uptake of the thymidine analog (see Fig. 8, Bagshawe et al, 1991). Also tumour to blood, colon and other tissue ratios remain approximately constant and do not deteriorate over this range of injected activity. If uptake does increase linearly with administered activity, then the MIRD doses given in Table II may be linearly scaled. For tumour toxicity this assumption may be untrue, because only that fraction of cells in S phase at, or shortly after, the moment of administration will incorporate the thymidine analog into their DNA. If the increase in uptake affects only the same small sub-set of cells, then overkill will occur, and there will be a saturation effect in the cell sterilization. This would need to be overcome by a fractionated administration of the thymidine precursor so as to spread the ^{125}IUdR incorporation as evenly over the cell population as possible. The difficulty that arises in this approach results from the short duration of the HU normal tissue cell block, which is maintained for about 1–2 hours, after which the tumour/normal tissue uptake ratios decline as the normal proliferating tissue cells come out of the block (Bagshawe et al, 1991). Repeated administrations of HU are possible only up to a total level of ~200 mg/kg, *i.e.* ~4 × 50 mg/kg required for the best tumour/normal tissue ratios, beyond which HU toxicity becomes a complication (Ijiri & Potten, 1987).

Dosimetry of ^{131}IUdR and ^{211}AtUdR: the cross-fire component

The major limitation of the proposed therapy with pure Auger-emitting thymidine precursors is the short range effects which limit toxicity to those cells which incorporate the radiolabelled analog. For this reason, two further radionuclides were included in the analysis: ^{131}I, a β-emitter of mean range 467 µm with a small unimportant component of Auger electrons from nuclear de-excitation by internal conversion (see Table I), and Astatine-211 (^{211}At), a source of Auger electrons but in addition an α-source of mean range $\sim 60\ \mu$m. These sources provide a much broader distribution of dose around the site of decay than with pure Auger sources. Studies by Hofer (1980) with ^{131}IUdR have not shown the enhanced radiotoxicity effects seen with ^{125}IUdR, demonstrating that any rise in toxicity resulting from β-emission within a DNA base is small. The tissue toxicity from ^{131}IUdR can therefore be assumed to be adequately accounted for by the tissue doses calculated using the MIRD formulation. The results (Table II) show tumour/blood and other tissue ratios of typically 3:5, reflecting the relative retention characteristics in the respective tissues relative to tumour.

Astatine-211 is a halogen which emits both Auger electrons and α-particles. It has a half-life of 7.2 hours, so that over 99% of the decays occur within typical human tumour cell cycle times. ^{211}AtUdR exhibits a high LET radiotoxicity up to a distance of 65 µm. Cells that fail to take up the thymidine precursor, because they do not enter S during the periods of administration, may be sterilized by the α-emissions from adjacent ^{211}At-loaded cells. Tissue doses from ^{211}AtUdR using MIRD are given in Table II (again based on the animal retention data for ^{125}IUdR) from a 1.85 MBq injection. All tissue doses are significantly higher per unit administered activity than for the other isotopes considered, because of the much greater emission energies involved. Mammalian cell survival data for exposure to α-particles generally yield D_0 values (the dose required to reduce a cell population to 37% survival) of between 0.5 Gy and 1.0 Gy (Barendsen, 1966; Thacker et al, 1979). Both blood and stomach doses are higher than the tumour. This is a result of the short half-life of ^{211}At, which biases the doses to tissues with high activities at early times after administration. Mice toxicity studies with ^{211}At (Cobb et al, 1988) show that the onset of chronic animal toxicity occurs at administered activities of ^{211}At in excess of 61 kBq/g (1.65 μCi/g). The normal tissue doses quoted are in principle survivable, provided they are not supplemented too greatly by effects due to DNA incorporation. The tumour burden, 0.53 Gy, would result in a reduction in cell population to between 40% and 60%, depending on the choice of D_0. For the tumour, assuming the ^{211}At is present predominantly in the DNA-bound form, there is the additional radiotoxicity resulting from the Auger electrons and the close proximity of the α-emission and associated recoil atom to the DNA target. Meyer et al (1975) have performed tissue retention measurements for astatinated uracil, ^{211}AtU, in melanoma-bearing mice and found no selective tumour cell incorporation. However, cell survival experiments have been performed with cell cultures exposed to an α-source (Barendsen, 1966; Thacker et al, 1979) as well as exposed to ^{211}At-labelled cell membrane-specific antibodies (Vaughan et al, 1982). Reports on the number of α-particle traversals of a cell nucleus for a 99% cell sterilization vary between 1 and 5 (Barendsen, 1966). The number of ^{211}At decays per gram of tumour corresponding to the dose calculated to the tumour in Table II is 4.9×10^8. Assuming 10^8 cells per gram of tumour, this would yield an average of ~ 5 decays per cell. This incorporation specific radiotoxicity is in addition to any tissue toxicity resulting from the MIRD tumour dose (the cross-fire component). The cytotoxicity to cells which incorporate ^{221}AtUdR has not to the knowledge of the authors been measured, but may be as low as 1 decay for a D_0 level of cell "kill". This source may yield a considerable improvement over the pure Auger sources, if the major limitation proves to be incorporation heterogeneity.

Conclusions

Administration of HU, 5-FU and methotrexate may be used to achieve selective uptake of radiolabelled thymidine analogs in resistant tumours. The short-range high radiotoxicity of Auger sources when incorporated with a high degree of specificity into the genetic material of the target cell, enables extremely high tumour/non-tumour ratios to be obtained. Uptake levels in tumour cell nuclei sufficient to produce in excess of 100 disintegrations per cell within the typical cell doubling time may be achievable at the expense of very low radiation doses of less than 0.01 Gy to the normal tissues. The major limitation of this technique is the heterogeneity of incorporation of the radiolabelled thymidine analog in the tumour cell population leading to severe microdosimetric problems in evaluating the radiotoxicity of the tumour.

Using the pharmacokinetic data of Bagshawe et al (1991) and the dosimetric data of this paper, one can estimate whether promising levels of tumour cell killing can be achieved at the measured differential level of ^{125}IUdR tumour uptake. It is assumed that a bone marrow dose of 50 cGy is dose limiting and that bone marrow specific activity levels are equal to those measured for blood. Using the most optimistic assumptions, all the ^{125}I is incorporated uniformly into the DNA of tumour cells but none into the DNA of the bone marrow stem cell population, then the administered dose could be escalated from 1.85 MBq to 356 MBq, assuming dose to bone marrow rises linearly with increasing administered activity. A uniform distribution of ^{125}IUdR incorporation in tumour following a 1.85 MBq administration would produce 26 decays/cell. This would rise to $192 \times 26 = 4608$ decays/cell, a number quite sufficient to kill all tumour cells. Using pessimistic assumptions, that the measured ^{125}I biodistribution in blood was a result of ^{125}IUdR incorporated in the bone marrow stem cells, a 1.85 MBq administration would correspond to 7.94 disintegrations/cell. If it is desired to keep the mean number of decays per bone marrow cell below 70 (to ensure not greater than 50% sterilization), the administered activity could be raised to $1.85 \times 70/7.94 = 16.30$ MBq. This would result in an increase in the average number of ^{125}I decays per tumour cell DNA to 212. Thus, a tumour cell sterilization down to 1.2% survival can be achieved, at the expense of a reduction in the bone marrow stem cells to 50%.

The above two estimates of tumour cell inactivation illustrate the range of possible values based upon extreme assumptions as to the fraction of ^{125}IUdR, present in blood, which becomes incorporated into the bone marrow stem cell population. The limit of thymidine analog which can be actually administered in a therapy protocol will critically depend on the actual fraction of thymidine analog incorporated into the normal tissues. In addition, the heterogeneity of incorporation of the thymidine analog into the normal dose-limiting tissues will affect the level of dose escalation possible before the onset of normal tissue toxicity. The level of tumour cell kill, resulting at the maximum tolerated dose of ^{125}IUdR, will be largely influenced by the actual fraction of cells that take up the thymidine precursor. This fraction can be improved by fractionated administrations.

The Auger sources ^{123}I and ^{77}Br have been assessed as possible alternatives to ^{125}I, which, because of their shorter half-lives, require far fewer radiolabels incorporated per cell DNA for the same cell toxicity. Radiation dose estimates for these Auger emitters are compared with dose calculations for ^{131}IUdR and ^{211}AtUdR, a β- and α-source, respectively, which can sterilize through radiation cross-fire cells that fail to take up the thymidine precursor. Astatine-211 looks especially promising since the short 60 μm range and high radiotoxicity of its α-emission may have a significant effect on surrounding tumour cells, possibly not incorporating any of the radiolabelled thymidine analog, and be short enough to minimize the non-specific cross-fire component in the non-tumour tissues.

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The effect of sodium iothalamate on the vascular resistance of the isolated perfused rat kidney

By J. L. Haylor, BPharm, PhD, A. A. El Sayed, MB, BCh, *A. M. El Nahas, FRCP, PhD and †S. K. Morcos, FRCS, FFRRCSI, FRCR

Department of Pharmacology and Therapeutics, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF and Departments of *Renal Medicine and †Radiodiagnosis, Northern General Hospital, Herries Road, Sheffield

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Abstract. The direct effects of sodium iothalamate on renal vascular resistance (RVR) were examined using the isolated perfused rat kidney experimental model. A concentration-dependent biphasic change in RVR was produced with the hyperosmolar solution of sodium iothalamate [(Conray 420), 420 mgI/ml, 2500 mOsmol/kg/H_2O]. The response characterized by an initial fall followed by a prolonged increase in RVR on discontinuation of the iothalamate infusion. No significant change in RVR was observed when iothalamate was infused as an iso-osmotic solution (60 mgI/ml, 280 mOsmol/kg/H_2O) at a rate of 0.525 ml/min. to produce a concentration of 4.2 mgI/ml in the renal perfusate. We conclude that sodium iothalamate can exert direct biphasic effects on RVR which are mediated by its hyperosmolality rather than its chemical content.

Acute renal dysfunction has been reported as an adverse effect following the intravascular administration of contrast media (Golman & Almen, 1985). Impaired renal perfusion has been proposed as one of the mechanisms mediating the nephrotoxicity of contrast media (Dawson, 1985). Animal studies have shown that contrast media produce an acute biphasic change in renal blood flow consisting of a large transient increase followed by a smaller, more prolonged decrease (Vari et al, 1988). The precise mechanism underlying the decrease in renal blood flow remains unknown. The hyperosmolality of contrast media has been implicated (Russell & Sherwood, 1974), although in other studies hyperosmolality and the reduction in renal blood flow appeared to be unrelated (Danford et al, 1969; Norby & Dibona, 1975). Some have suggested an indirect effect through a reduction in cardiac output (Higgins, 1980) and peripheral vasodilatation (Dawson & Edgerton, 1983). Others have postulated a direct effect on the renal vasculature. A role for systemic hormones such as antidiuretic hormone (ADH) (Trewhella et al, 1990) or autocoids such as adenosine (Arend et al, 1987; Deray et al, 1989) have been put forward while a role for increased intrarenal interstitial pressure has also been postulated for the decrease in renal blood flow (Katzberg et al, 1982). The precise mechanism and mediators involved, however, remain to be determined.

In vivo studies in experimental animals have so far failed to dissociate the systemic effects of contrast media on renal function from direct effects on the kidney. In this study, we have used a new experimental approach relying on the isolated perfused rat kidney (IPRK) to determine whether sodium iothalamate can exert a direct effect on renal vascular resistance.

Materials and methods

Male wistar rats (250–300 g), given an intraperitoneal injection of heparin 1000 international units, were killed by cervical spine dislocation. The left kidney was removed and the left renal artery cannulated. Kidneys ($n = 5$) were perfused in a non-recirculating system (Fig. 1), at constant flow (7.5 ml/min), with a Krebs/Henseleit solution gassed with 95% O_2/5% CO_2 at 37°C using a peristaltic pump. The renal perfusion pressure was continuously monitored using an electronic pressure transducer (Statham). Since the kidneys were perfused at constant flow, changes in renal perfusion pressure were directly proportional to changes in renal vascular resistance (RVR). The basal renal perfusion pressure was constant throughout each experiment varying between 60 and 80 mmHg in different preparations. Each kidney was equilibrated for a 30-minute period prior to the addition of sodium iothalamate via a syringe pump linked to the perfusion line (Fig. 1). Recovery to baseline was obtained between individual infusions in any one preparation. The contrast media solution in the syringe pump is termed the *infusate*, while the solution perfusing the kidney is termed the *renal perfusate*.

Concentration response experiments were performed in each preparation. A 70% solution of sodium iothalamate (Conray 420) was infused into the perfusate line for 10-minute periods at predetermined rates to produce a range of iothalamate concentrations in the renal perfusate varying from 0.07% to 4.2% (Table I). The sodium

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Address for correspondence: Dr S. K. Morcos, X-ray Department, Northern General Hospital, Herries Road, Sheffield 5.

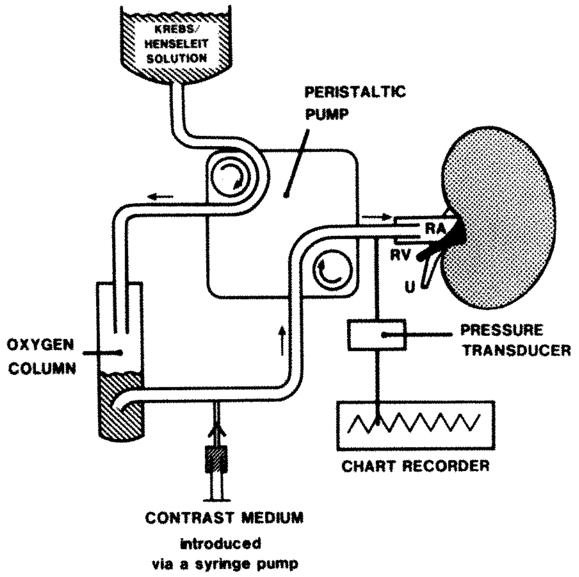

Figure 1. Schematic diagram for the non-recirculating model of the isolated perfused rat kidney (IPRK). Sodium iothalamate was added to the Krebs/Henseleit solution by continous infusion using a syringe pump. The solution in the pipe line beyond the peristaltic pump is referred to as renal perfusate which flows into the kidney at a constant rate of 7.5 ml/min. Arrows indicate the direction of flow. (RA = renal artery; RV = renal vein; U = ureter.)

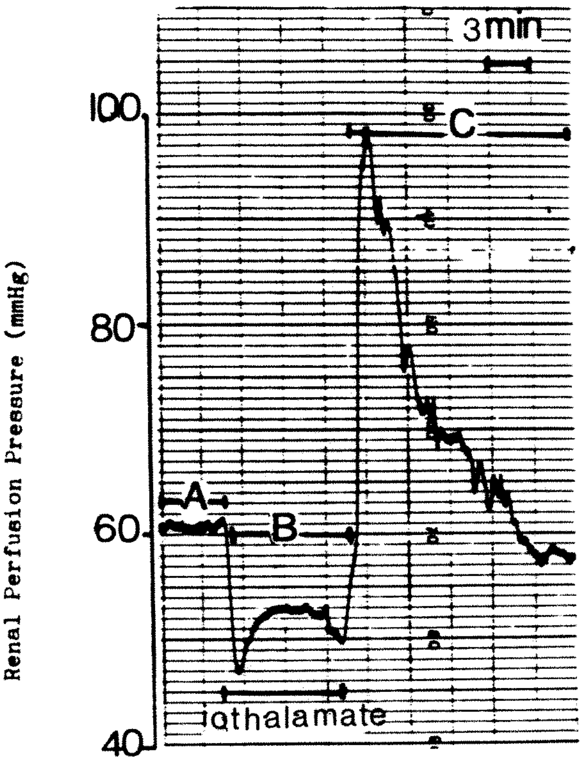

Figure 2. Sample tracing for the effect of a 10-minute infusion of hyperosmotic solution of sodium iothalamate (4.2%, 25 mgI/ml) on renal perfusion pressure in the IPRK. A is the basal perfusion pressure (60 mmHg), B the fall in perfusion pressure during iothalamate infusion and C the rise in perfusion pressure after the discontinuation of iothalamate; the perfusion pressure then gradually returned to its basal value.

iothalamate was added to the perfusion line at a point prior to the peristaltic pump to avoid altering the rate of perfusate flow through the kidney. The osmolality of the renal perfusate was measured using a freezing point depression osmometer (Roebling). In the absence of iothalamate, the osmolality of the Krebs/Henseleit perfusate was 280 mOsm/kg/H_2O. In this experiment, iso-osmolar solutions had the same osmolality as the Krebs/Henseleit solution, *i.e.* 280 mOsm/kg/H_2O.

The contribution of hyperosmolality to the change in RVR produced by sodium iothalamate concentration of 0.7% in the renal perfusate was also examined in each preparation. An iso-osmolar solution of sodium iothalamate was prepared by diluting Conray 420 solution with distilled water. The new solution contained 60 mgI/ml but was iso-osmotic with the Krebs/Henseleit solution. This iso-osmotic solution was infused for 10 minutes into the perfusion line at seven times the rate of delivery of the Conray 420 to achieve the same total dose per unit time of iothalamate delivered to the kidney (Table I). The renal perfusate flow rate was constant at 7.5 ml/sec. The use of iso-osmolar solution of sodium iothalamate produced a greater dilution of the Krebs/Henseleit solution perfusing the kidney than neat Conray 420. However, this degree of perfusate dilution had no effect on renal vascular resistance per se.

The results were compared using a paired Student's *t*-test (Microtab).

Table I. Syringe pump infusion rates required to produce the given concentrations of iothalamate perfusing the kidney; (a) infusing a neat solution of Conray 420 and (b) infusing an iso-osmolar solution of sodium iothalamate

Infusion rate (ml/min)	Iothalamate concentration in the renal perfusate		Measured osmolality of the renal perfusate (mOsmoles/kg/H_2O)
	(% iothalamate)	(mgI/ml)	
(a) Hyperosmolar solution of sodium iothalamate (420 mgI/ml "Conray 420")			
0.0075	0.07	0.42	281
0.0225	0.21	1.26	285
0.045	0.42	2.52	290
0.075	0.70	4.20	298
0.225	2.10	12.60	333
0.450	4.20	25.20	398
(b) Iso-osmolar solution of sodium iothalamate (60 mgI/ml)			
0.525	0.70	4.20	280

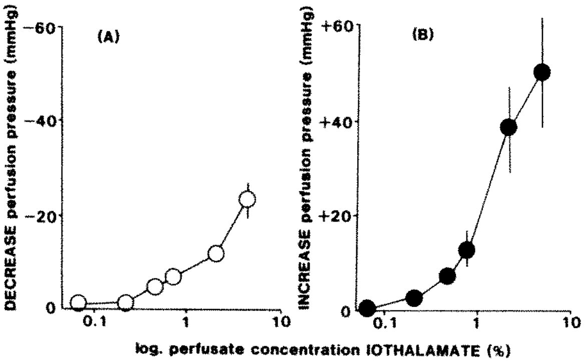

Figure 3. Concentration–response relationship to (A) the immediate decrease (○) in perfusion pressure produced by hyperosmotic solutions of iothalamate in the IPRK and (B) the delayed increase in perfusion pressure (●) produced immediately on stopping the iothalamate infusion. Vertical bars indicate standard error of the mean (SEM); where absent, the SEM is within the data point ($n = 5$).

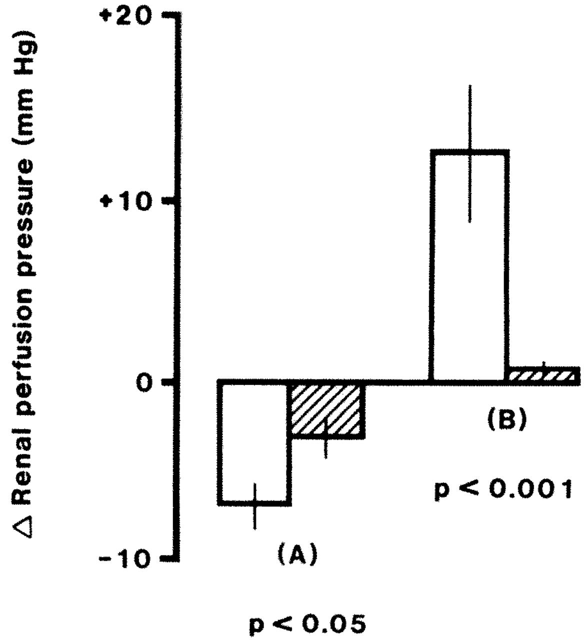

Figure 5. Comparison between the ability of iothalamate (0.7%, 4.2 mgI/ml) (A) to decrease and (B) to increase renal perfusion pressure when delivered to the kidney as either a hyperosmotic (unhatched) or an iso-osmotic (hatched) perfusate. Vertical bars indicate the SEM ($n = 5$). (Δ = change in perfusion pressure.)

Results

All kidneys ($n = 5$) showed a biphasic response to the infusion of a hyperosmotic solution of sodium iothalamate. A sample recording of the change in renal perfusion pressure produced by a 10-minute infusion of sodium iothalamate (4.2%, 25 mgI/ml) is shown in Fig. 2. The response consisted of an immediate fall in perfusion pressure which gradually returned towards its baseline, while sodium iothalamate remained in contact with the kidney. When the infusion of sodium iothalamate was discontinued, an increase in renal perfusion pressure was observed which at this dose took up to 20 minutes to return to its baseline. A pilot series of experiments showed that a 10-minute contact time between iothalamate and the kidney was required before the maximum increase in perfusion pressure following discontinuation of the iothalamate infusion could be demonstrated. A concentration–response relationship was observed between both the increase and the decrease in renal perfusion pressure produced by iothalamate (Fig. 3), both responses increasing with the increase in perfusate osmolality (see Table I).

In order to identify the contribution of osmolality to the renal response produced by iothalamate, the effect of iothalammate 0.7% (4.2 mgI/ml) was compared when delivered to the kidney in either a hyperosmotic (298 mOsm/kg/H_2O) or an iso-osmotic (280 mOsm/kg/H_2O) perfusate (Table I). Sample recordings from a single experiment are shown in Fig. 4. The increase in renal perfusion pressure following discontinuation of the iothalamate infusion was completely absent when the iso-osmotic solution was employed. The initial fall in renal perfusion pressure induced by iothalamate was also significantly reduced following the iso-osmotic solution of iothalamate but not completely abolished (Fig. 5).

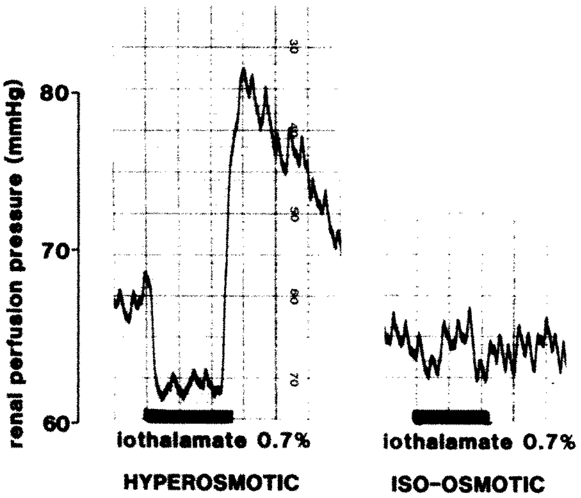

Figure 4. Sample tracing for the comparison between the effect of iothalamate (0.7%, 4.2 mgI/ml) on renal perfusion pressure when delivered as either a hyperosmotic (298 mOsm/kg/H_2O) or an iso-osmotic (280 mOsm/kg/H_2O) perfusate. No increase in renal perfusion pressure is seen with the iso-osmotic solution. The thick black line (■) indicates the infusion period of the iothalamate solution.

Discussion

The decrease in renal perfusion pressure produced by sodium iothalamate in this IPRK model demonstrates that contrast media can reduce renal vascular resistance (RVR) by a direct effect on the kidney. Both the onset and the offset of this response were very rapid, the maximum response to a single concentration occurring within 5–10 seconds of infusion into the kidney. The marked increase in RVR observed on discontinuation of the iothalamate infusion was attributed to a direct increase in RVR produced by sodium iothalamate which, however, was much slower in both its onset and its offset than the initial fall. The slow onset of this effect was demonstrated in a pilot series of experiments where a 10-minute contact time was necessary to demonstrate the maximum increase in RVR to a single concentration of iothalamate. Sodium iothalamate therefore produced a biphasic, concentration-dependent change in RVR, *i.e.* a decrease followed by a slower increase. However, during the iothalamate infusion, the net effect was to decrease RVR under the conditions employed. The later increase in RVR to iothalamate could not be explained as an overshot or rebound phenomena in response to the initial fall in RVR since it cannot be demonstrated with standard vasodilators such as atrial natriuretic peptide in this preparation (Burton et al, 1990).

The ability to withdraw iothalamate immediately from the kidney was a feature of our non-recirculating perfusion system which cannot be paralleled *in vivo*. *In vivo*, an acute biphasic change in renal vascular resistance has also been described following contrast media administration which consisted of a large transient increase in renal blood flow followed by a slower more prolonged fall (Russell & Sherwood, 1974; Vari et al, 1988). However, *in vivo*, contrast media do not always produce a delayed fall in renal blood flow to below baseline values following intravenous administration (Katzberg et al, 1986), although the transient nature of the initial increase in renal blod flow has consistently been observed.

The absence of any change in RVR to a 0.7% iso-osmotic solution of sodium iothalamate implies that such responses are a direct consequence of the high osmolality of the contrast medium. The use of iothalamate as its own osmolal control was more accurate in our view than the use of so-called "inert" hyperosmotic agents such as mannitol which are known to have other pharmacological properties such as the ability to scavenge free radical hydroxyl ions (Rosenblum, 1983; MacGovern et al, 1984). However, the concentration of iothalamate at which this procedure could be examined was limited since the greater dilution of the Krebs/Henseleit perfusate which would occur at higher iothalamate concentrations would begin to modify renal vascular reactivity directly.

The renal response to iothalamate described in the present experiments could not be mediated by a systemic effect such as a change in plasma ADH (Trewhella et al, 1990), a change in cardiac output (Higgins, 1980), peripheral vasodilatation (Dawson & Edgerton, 1983) or a change in the sensitivity of the kidney to a systemic stimulus since an isolated perfusion system was employed. However, our experimental approach does not allow us to distinguish between the three mechanisms postulated to explain renal vasoconstriction induced by hypertonic solutions *in vivo*. These suggested mechanisms include (1) the release of a renal vasoconstrictor agent, (2) an increase in intrarenal interstitial pressure or (3) a unique response of vascular smooth muscle in the kidney (Katzberg et al, 1982). In addition, the possibility that the direct renal effects of sodium iothalamate may be modified *in vivo* by other systemic properties cannot be excluded.

The IPRK model as demonstrated here offers the opportunity of separating the local effects of contrast media on the kidney from their systemic actions. From the present study, however, it is important to emphasize that the renal effects of iothalamate delivered as an iso-osmotic solution were only investigated at a single concentration 4.2 mgI/ml perfusing the kidney. This concentration is comparable to the peak plasma levels of contrast media attained following the intravenous administration of 100 ml Urografin 370 in man (Feldman et al, 1984). It is possible that higher doses of iothalamate, such as those used in aortography or renal arteriography, could exert further effects on kidney function through additional direct chemical properties.

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Case reports

Splenic calcification following treatment of Hodgkin's disease

By A. R. Moody, MA, MRCP, FRCR and D. M. King, MB, DMRD, FRCR

Department of Radiology, Royal Marsden Hospital, Fulham Road, London SW3 6JJ

(Received March 1990 and in revised form June 1990)

Keywords: Hodgkin's disease, Splenic calcification, Computed tomography, Ultrasound, Chemotherapy

Calcification within the spleen has many different manifestations and aetiologies. We report a single case of a patient with Stage IV Hodgkin disease who developed splenic calcification following chemotherapy. A search of the literature has failed to reveal a previous report of this phenomenon.

Case report

A 43-year-old man presented with a 6-month history of increasing painless swelling in the left side of his neck. Latterly this had been accompanied by the development of further smaller cervical nodules. He was otherwise asymptomatic.

On examination, mobile rubbery lymph nodes were confirmed in the left cervical and supra-clavicular regions, the largest being up to 1 cm in diameter. Smaller nodes were also found in the left axilla and both inguinal regions. One of the nodes in the left posterior cervical triangle was removed and histological examination revealed mixed cellularity Hodgkin disease.

A plain radiograph of the chest demonstrated no abnormality and computed tomography (CT) of the thorax and abdomen was performed to delineate the extent of the disease. There was no evidence of mediastinal or other lymph node enlargement; the liver and spleen were normal in size and shape and contained no focal abnormality (Fig. 1). A bipedal lymphogram was performed which demonstrated an unusual and suspicious appearance in the proximal inguinal regions. Lymph node biopsy revealed no evidence of disease. The patient was therefore staged as IA mixed cellularity Hodgkin disease.

He began a course of radiotherapy in the modified upper mantle regime, which included the mediastinum and both sides of the neck, but excluded the axillae. A single anterior field, with posterior mediastinal boost, delivered 4000 CGy to the skin anteriorly, and a 3600 CGy does to the tumour in a 6-week period. Treatment was uneventful and the lymph node enlargement rapidly resolved.

Four months after completion of therapy, the patient re-presented with lymph node enlargement in the left axilla. Computed tomographic examination was again unremarkable; the chest was clear and liver and spleen remained normal in size and shape, with no focal abnormality. The alkaline phosphatase was persistently elevated and an abdominal ultrasound examination was therefore performed. Although no liver abnormality was shown, it did demonstrate several clearly marginated, echo-poor foci within a normal sized spleen (Fig. 2); these were most consistent with small lymphomatous deposits.

Address for correspondence: Dr D. M. King, Department of Diagnostic Radiology, Royal Marsden Hospital, Fulham Road, London SW3 6JJ.

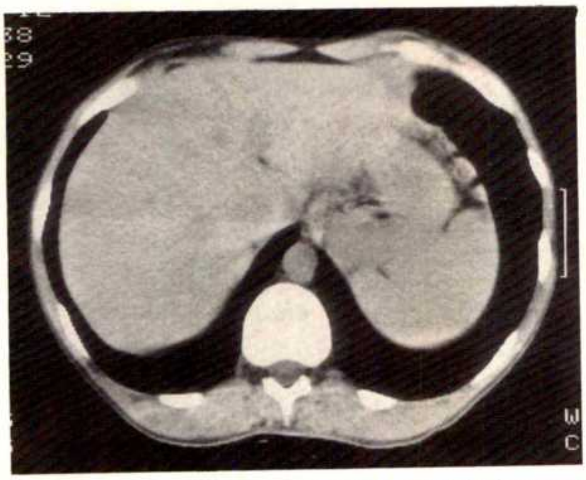

Figure 1. Computed tomography section through the upper abdomen before treatment. The spleen appears of homogeneous parenchymal density.

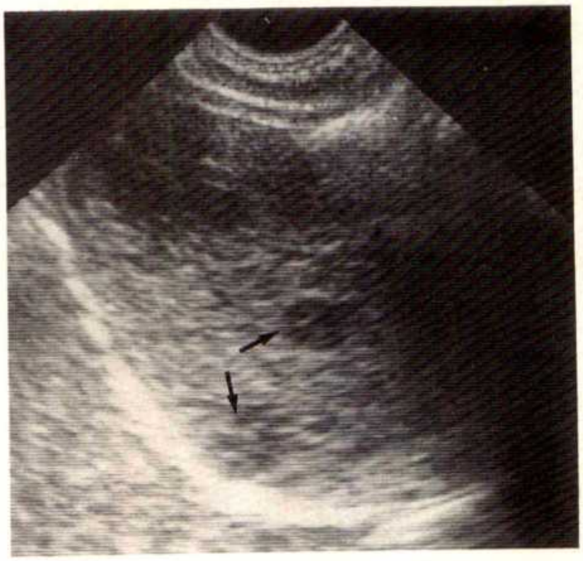

Figure 2. An oblique sonogram demonstrating abnormal echo-poor foci within the spleen, consistent with involvement by lymphoma (arrows).

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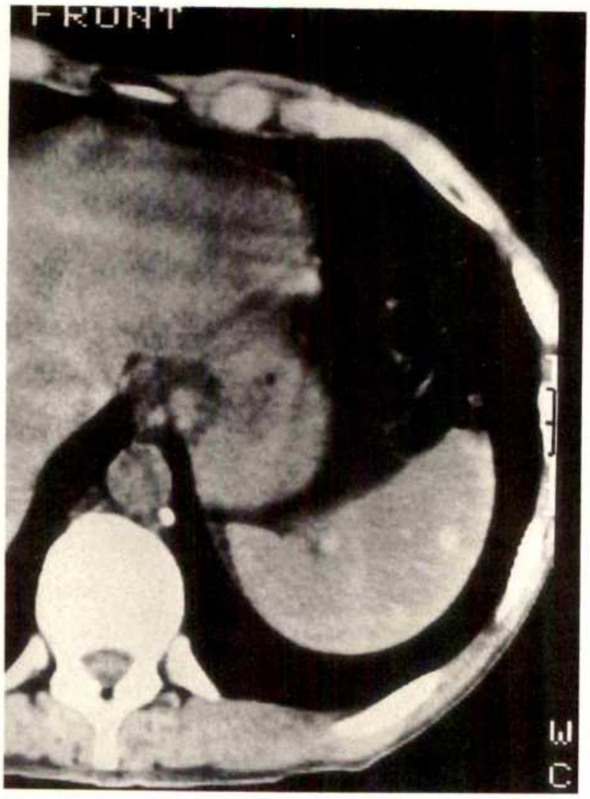

Figure 3. Amorphous calcification within the spleen on CT section 1 month after completion of chemotherapy.

Following restaging, combination chemotherapy was instituted using the CHLOROPP regime (Chlorambucil and Procarbazine orally for 10 days, with prednisolone orally for 14 days and Vincristine intravenously on Days 1 and 8). Complete remission was achieved within 4 weeks, but chemotherapy was continued for a total of 5 months.

A further CT examination demonstrated no evidence of lymphoma, but foci of calcific density were now apparent in the spleen, not present on the pre-treatment studies (Fig. 3). The patient remains well.

Discussion

There are many different causes of calcification within the spleen (Reeder & Felson, 1975), but a search of the literature has failed to reveal a reference to its association with treated Hodgkin disease.

Punctate calcification within the parenchyma, as with this case, may be associated with phleboliths and haemangiomata; it is also seen in tuberculosis and histoplasmosis, and occasionally follows *Armillifer armillatus* infestation or cysticercosis. Tuberculous calcification is, however, usually accompanied by hepatic or nodal calcification.

More diffuse, granular calcification may be associated with splenic infarction, as in sickle cell disease, and has also been reported in carcinoma of the ovary, bowel and breast. Parenchymal calcification may be mimicked by previous Thorotrast administration. Calcification on the surface of the spleen may follow subcapsular haemorrhages, and cysts may calcify, exhibiting a typical curvilinear appearance. Splenic artery and aneurysm calcification is not infrequent but is usually clearly outside the splenic parenchyma.

In addition to demonstrating a new feature in the treatment of Hodgkin disease, this case also illustrates the poor sensitivity of CT in detecting focal involvement of the spleen by lymphoma (Castellino et al, 1984). The complementary role of ultrasound in the staging of patients with Hodgkin disease, particularly when there is clinical or CT suspicion, is further emphasized.

Acknowledgments

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Well ventilated bullae: a potential confusion on ventilation/perfusion scanning

By *Deborah A. Cunningham, MRCP, FRCR and †David M. Mitchell, MD, MRCP

Departments of Clinical Physics and †Medicine, St Mary's Hospital, Praed Street, London W2, UK

(Received March 1990 and in revised form May 1990)

Keywords: Ventilation/perfusion scanning, Pulmonary embolism, Chronic obstructive airways disease

Isotope lung scanning is the only non-invasive test capable of making the diagnosis of pulmonary embolism reliably. While defects of perfusion have many causes (Wagner & Strauss, 1975) combining a perfusion lung scan with images of regional ventilation increases specificity, such that segmental or larger defects of perfusion unmatched in ventilation are taken as strong evidence in favour of the diagnosis of pulmonary embolus ("high probability") (Biello et al, 1979).

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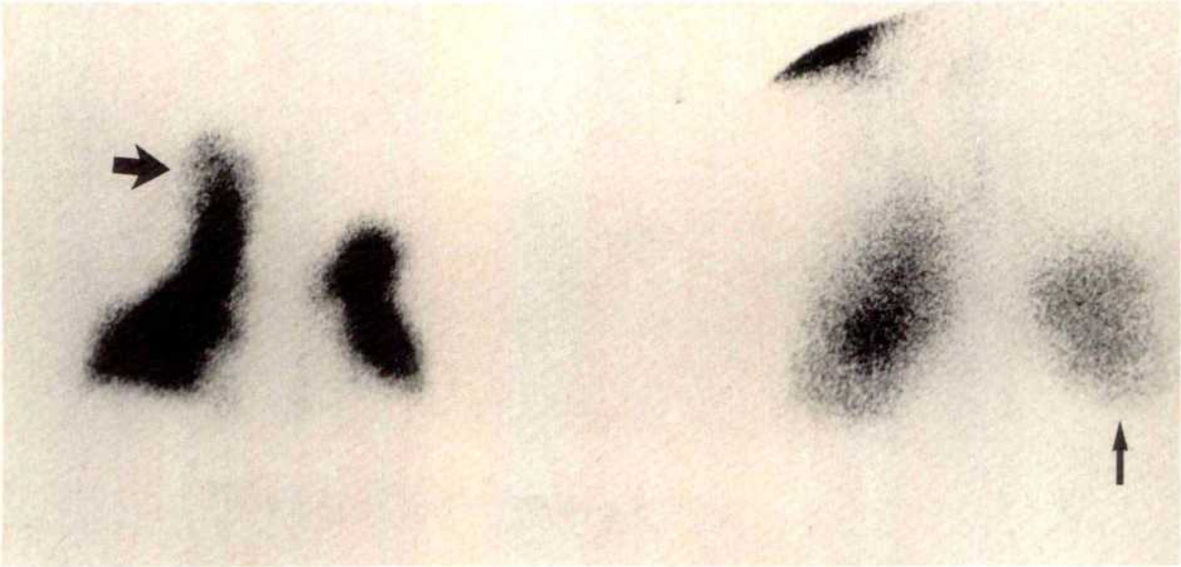
*Author for correspondence and reprint requests.



(a)

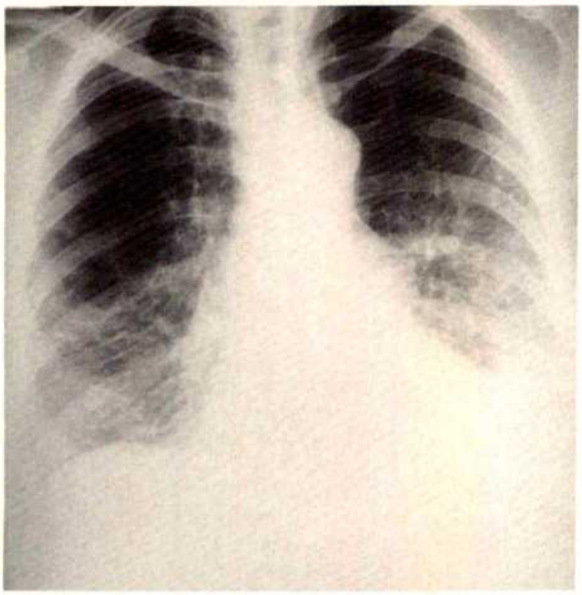


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Figure 1. (a) Ventilation/perfusion scan showing unmatched defect of perfusion in the right upper lobe. (b) Chest radiograph showing bullous change in this area.

In the present paper we report three cases in which bullous areas showed normal ventilation with Krypton 81m and absent perfusion, resulting in large areas of ventilation/perfusion mis-match.

Case reports

Case 1

A 65-year-old female Irish betting clerk was admitted with a Staphylococcal septicaemia following a boil on her elbow. She had no respiratory symptoms but she was known to have basal lung fibrosis and a chest radiograph showed apical bullae with bilateral basal fibrosis. During her admission she developed acute left sided pleuritic chest pain and a chest radiograph showed a small left pleural effusion. The diagnosis of pulmonary embolism (PE) seemed likely and a ventilation/perfusion lung scan was performed using Technetium-99m macro aggregates and Krypton 81m gas.

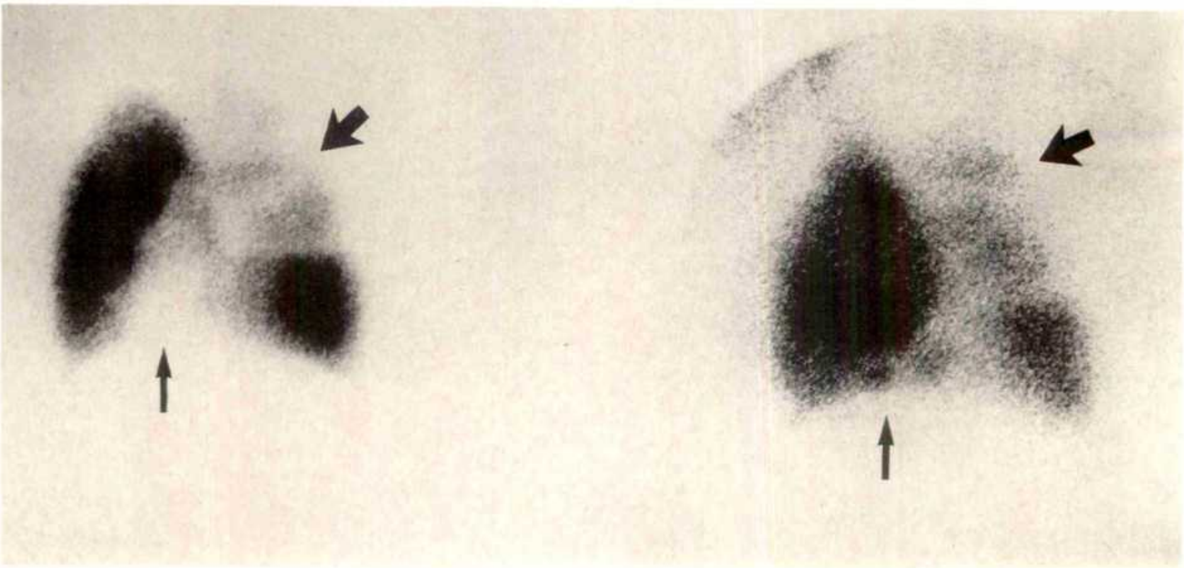
As expected the bullae in the left apex showed matched defects of ventilation and perfusion. In the right mid-zone, however, there was a large area of ventilation/perfusion mis-match, corresponding to a region of bullous formation on radiography (Fig. 1). A moderate sized mis-matched defect in the left mid-zone probably corresponded to a bullous area also, but PE could not be excluded. The patient was anticoagulated on clinical grounds.

Case 2

A 36-year-old hospital cleaner with known cystic bronchiectasis was referred for a lung scan after the sudden onset of left sided pleuritic chest pain. Multiple matched defects were present in the right lung corresponding to cystic areas on chest radiography (Fig. 2). At the left base a large area of ventilation/perfusion mis-match was present corresponding exactly to a large solitary bulla in the left lower lobe. The rest of the left lung was normally perfused and PE seemed unlikely. Her pain persisted over months and a final diagnosis was of musculoskeletal pain.

Case 3

A 35-year-old Moroccan man presented with severe pulmonary TB. During the course of his illness the apical cavities became thin walled and persistent, finally resembling thin-walled bullae. Fifteen months after the initial presentation a ventilation/perfusion scan was ordered to assess regional lung function. There was no clinical suggestion of PE. In the left


(a)

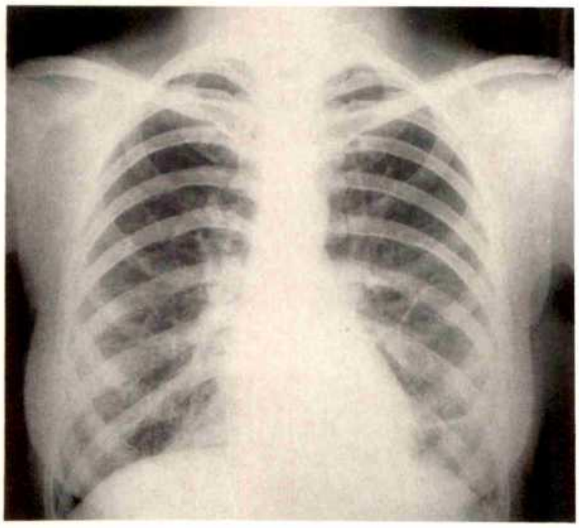

(b)

Figure 2. (a) Ventilation/perfusion scan showing matched defects of ventilation/perfusion in the right upper lobe (large arrow) and unmatched defect of perfusion in the left lower lobe (small arrow). (b) Chest radiograph showing left lower lobe bulla.

apex the bullae showed matched ventilation/perfusion defects as expected, but at the right apex where virtually the whole upper lobe was involved in bullous change there was no perfusion but apparently normal ventilation (Fig. 3). Xenon 133 scanning with wash out curves showed an almost normal rate of Xenon 133 clearance from the right apex.

Discussion

The three cases presented illustrate the fact that bullae may be well ventilated and hence result in ventilation/perfusion mis-match on lung scanning.

Bullous disease of the lung is common in the West, frequently as part of chronic obstructive airways disease (COAD) (Bates et al, 1971). When bullae form, the vessels that normally supply that part of the lung are displaced or destroyed and this results in a perfusion defect on a lung scan.

Most bullae are also under ventilated but the reason for this poor ventilation is complex. Under ventilation may be caused by obstruction of the normal airways supplying that part of the lung. This is said to be the case when bullous disease is seen in the setting of COAD, where obstruction of the airways is felt to be the primary aetiological factor in the development of bullae (McLean, 1958). Despite this obstruction, bullae remain inflated due to collateral air drift, but the rate of ventilation within them is markedly reduced resulting in a ventilation defect on Krypton 81m lung scanning, and this defect typically matches defects of perfusion (Cunningham & Lavender, 1981). In other settings, particularly in fibrotic lung or isolated bullous disease, obstruction to the airway may not play any part in the aetiology of bullous formation and it is then theoretically possible for ventilation to be maintained at a normal or near normal rate. This, however, is not common because of the loss of normal elastic recoil in the area of lung affected by bullous change. Thus, although air may enter the bullae on inspiration, the bullae will not collapse on expiration and air remains effectively trapped in this area. Hence regional ventilation is reduced.

For ventilation to be maintained as it appears to have been in our cases, continuity with the airway must have been maintained as well as normal or near normal lung elasticity. In all three cases, other areas of lung with

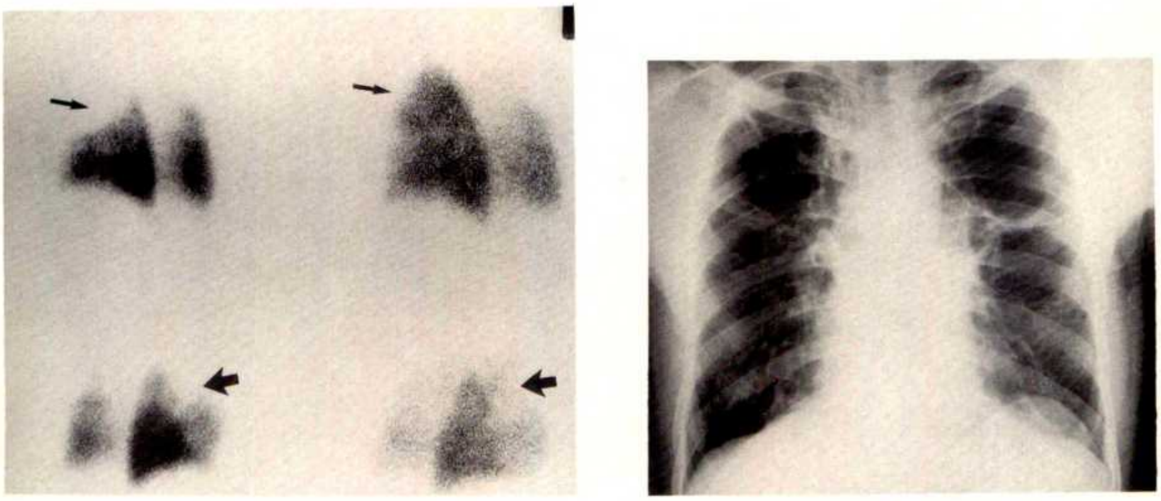

(a) (b)

Figure 3. (a) Ventilation/perfusion scan showing an unmatched defect in the left upper lobe (small arrow) and a matched defect of perfusion in the right upper lobe (large arrow). (b) Chest radiograph showing bilateral apical bullae.

apparently similar abnormalities radiologically showed matched defects of ventilation and perfusion, indicating that the maintenance of elasticity was patchy in the diseased portions of the lung.

Bullous disease may be investigated with a lung scan when surgical resection is being considered for the relief of symptoms, as in the third case. The main value of this investigation is in the demonstration of normal lung away from the site of bullous change, as patients in whom bullous disease is part of widespread COAD do not do well with surgery (Pride et al, 1970). Where the rest of the lung appears normal, bullae usually cause symptoms by compressing the surrounding healthy lung. In the case of large well ventilated but under perfused areas of lung, physiological dead space would be increased and this in itself could result in symptoms. In fact an increase in physiological dead space is unusual in bullous disease, reflecting the rarity of well ventilated bullae (Pride et al, 1973).

Two of the three patients were referred because of symptoms suggestive of PE. In a widely used scheme for the interpretation of lung scans, a single large unmatched defect of perfusion results in the patient being classified as "high probability" for PE (Biello et al, 1979). There are, however, other causes of ventilation/perfusion mis-match including carcinoma of the bronchus, lung fibrosis and lymphangitis carcinomatosa (Li et al, 1978; Datz, 1980). Most of these are readily apparent from the clinical setting and chest radiography. However, bullae are usually silent clinically unless widespread or occurring as part of COAD (Laurenzi et al, 1962), and the chest radiograph is known to be very insensitive at diagnosing bullous disease (Laws & Heard, 1962), so the possibility for confusion on ventilation/perfusion scanning exists. Fortunately, in the cases described, bullae were actually visible on the chest radiograph, corresponding to the areas of ventilation/perfusion mis-match.

The most common cause of bullous disease is COAD. If well ventilated bullae were frequent, one would expect the literature to reflect this by documenting a low specificity for the diagnosis of PE in the presence of COAD, but this is not the case (Taplin & Chopra, 1978). The explanation for this may lie in the suggested obstructive aetiology of bullous disease in this setting.

The cases presented indicate that, despite the rarity of well ventilated bullae, one should be aware of the possibility of ventilation/perfusion mis-match occurring in bullous disease, particularly when it is not part of COAD.

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Cranio-facial melorheostosis: case report and review of the literature

By J. W. Williams, FRCS, D. Monaghan, MRCP and N. A. Barrington, FRCR

Department of Radiology, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF

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Keywords: Melorheostosis, Cranio-facial

Melorheostosis is a rare condition principally affecting the bones of the appendicular skeleton, producing characteristic radiographic features of flowing "candle wax" subperiosteal bone and streaky endosteal bone formation in the diaphysis and epiphysis, which may affect only one side of long bones within a limb. Radiographic appearances form the basis of the diagnosis, as clinical and histological findings are non-specific.

Case report

Our patient, an elderly woman, was admitted from the Casualty Department following a fall. Radiographs of her pelvis and left elbow were obtained (Figs 1 and 2) showing the typical longitudinal distribution of flowing subperiosteal and endosteal new bone. The left wrist and right elbow were similarly affected, but to a lesser extent. Skull radiographs showed (Fig. 3) bony obliteration of the left maxillary antrum without expansion of its outline, thought to be due to melorheostosis and similar in appearance to a previously described case. Thickening of the vault may be partially due to hyperostosis frontalis interna, but is asymmetrical, and melorheostosis was suspected in addition.

Examination revealed no skin changes, vascular abnormalities or joint deformity and the patient had experienced no pain in the affected areas.

Discussion

Over 200 cases have now been reported. The classic pattern of subperiosteal bone deposition may be monostotic, polyostotic, monomelic or affect multiple limbs and the trunk (Morris et al, 1963). Extra-osseous bone deposition can occur. The linear distribution, often affecting only one side of a long bone, has been attributed to the distribution of the spinal sensory nerves (Murray & McCredie, 1979), though a rival theory

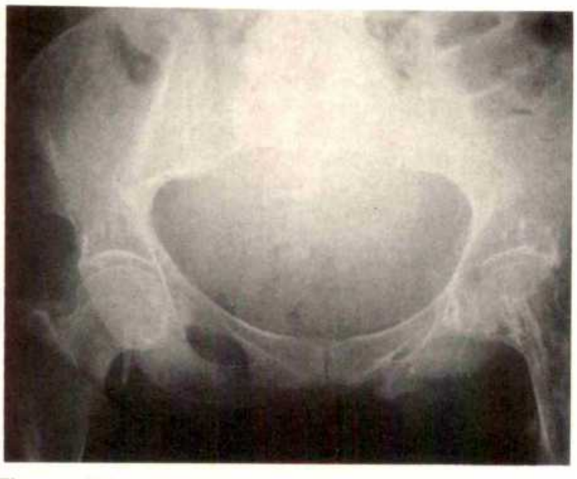


Figure 1. Pelvis showing changes of melorheostosis.

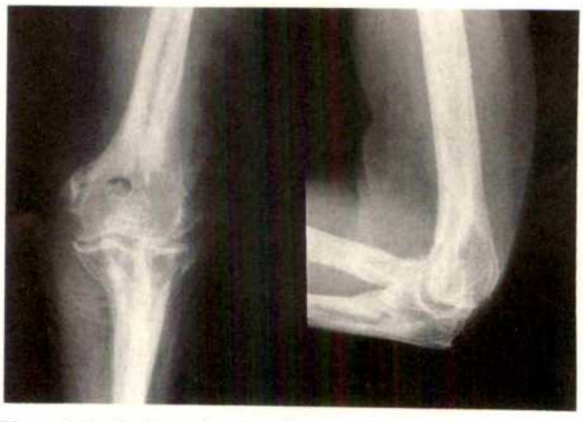
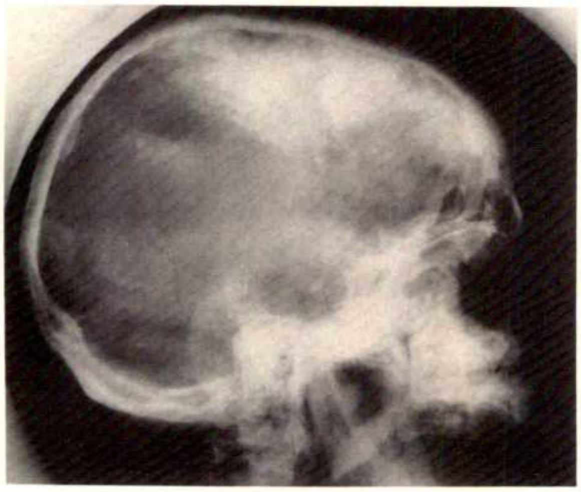
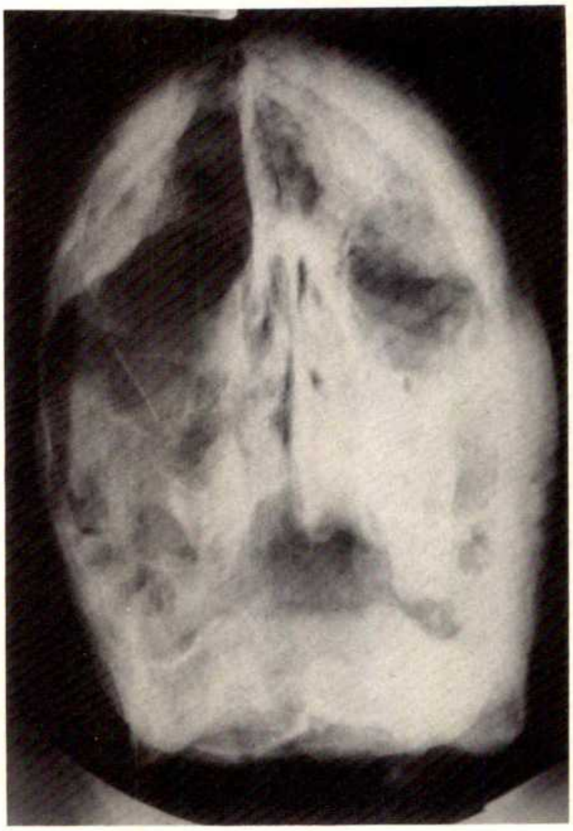


Figure 2. Left elbow showing changes of melorheostosis.



(a)



(b)

Figure 3. (a) Lateral and (b) frontal view of skull.

suggests that the appearance may be the result of a mesodermal disorder arising prior to limb bud formation in the embryo (Campbell et al, 1968).

In the young, presentation may involve limb length discrepancy or joint contractures refractory to standard soft tissue release procedures. Hypophosphataemic rickets has also been described (Lee & Sanderson, 1989). Radiographic features include streaky or patchy endosteal sclerosis, with later subperiosteal bone deposition (Younge et al, 1979).

Many older patients present with pain in the affected limb which can be difficult to treat and may respond to Nifedipine (Semble et al, 1986). Vascular abnormalities resembling linear scleroderma are well recognized associations. More recently, cases have been described in association with intradural, extra-medullary lipoma (Raby & Vivian, 1988) and osteosarcoma (Bostman et al, 1987). There is increased uptake on bone scan, and computed tomography (CT) scanning demonstrates the process well (Dimar & Campion, 1987).

Cranio-facial melorheostosis is unusual: of the 131 cases collected by Morris (Morris et al, 1963), only four affected the skull and one the face. Further cases with cranio-facial involvement have been described by Lievre (Leivre et al, 1959), and more recently by Caroli (Caroli et al, 1987) which includes an illustration of appearances on CT scanning.

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Lymphangiohaemangioma of the mediastinum

By Rosemary Toye, MA, MB, BS, Peter Armstrong, MB, BS, FRCR and Janet E. Dacie, FRCP, FRCR

Academic Department of Radiology, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE

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Keywords: Lymphangiohaemangioma, Mediastinal tumours

Lymphangiohaemangiomas are rare congenital malformations, which on histological examination show both vascular and lymphatic elements. Clinically they tend to behave as lymphangiomas. Conservative management is usually recommended, with intervention only if vital structures are affected or if required for cosmetic reasons (Bruce Williams, 1981). Mediastinal lymphangiohaemangiomas are exceedingly rare and may require treatment because of their position.

A case of benign lymphangiohaemangioma of the mediastinum is presented. Unlike the only previously reported case of computed tomography (CT) in this condition (Angtuaco et al, 1983), our case showed neither near-water density nor contrast enhancement following intravenous contrast medium administration.

Case report

A girl of 2 years and 8 months was admitted to Queen Elizabeth Hospital, Hackney, with a discharging cervical tuberculous fistula. She was incidentally found to have a superior mediastinal mass. After treatment of her tuberculosis, at the age of 2 years and 10 months, an exploratory thoracotomy was performed at Great Ormond Street Hospital. The operative findings were of an irresectible tumour densely adherent to the pericardium and to the great vessels in both thoracic cavities. Histological specimens showed a complex vascular malformation predominantly of lymphangiomatous tissue but containing abnormal blood vessels, appearances consistent with a diagnosis of benign lymphangiohaemangioma. A subtotal resection was performed at the age of 3 years 4 months. The left phrenic nerve was noted to pass through part of the tumour and had to be resected.

At 4 years and 7 months the patient presented with a persistent cough. Compression of the trachea was noted on barium swallow examination and engorged superficial veins were observed over the upper left chest wall. The cough resolved spontaneously so no further treatment was given.

As an adolescent she began to experience shortness of breath on exertion which increasingly restricted her activity. The plain chest radiograph (Fig. 1) and CT scans (Figs 2 and 3) when she was 15 years old showed a large mass filling the upper two-thirds of the left hemithorax. It showed extension into the neck, encasement and compression of the left subclavian and brachiocephalic veins, the left common carotid artery and the

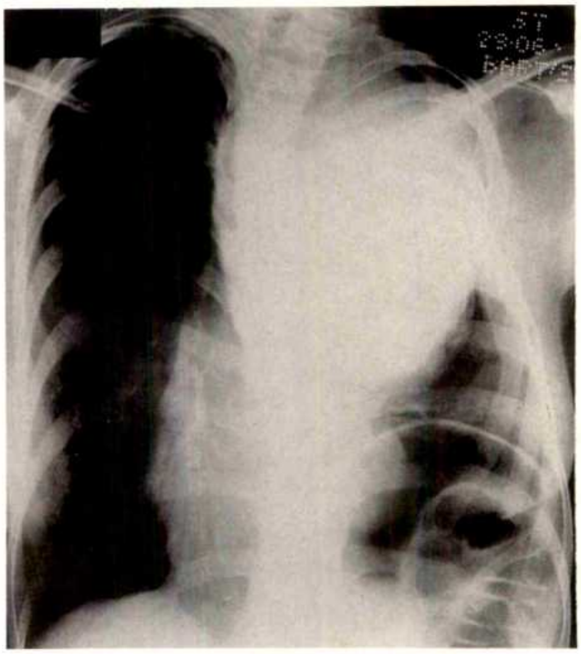


Figure 1. Chest radiograph demonstrating a large left-sided mediastinal mass with elevation of the left hemidiaphragm, rib deformity and thoracic scoliosis.

Address correspondence to: Professor P. Armstrong, Academic Department of Radiology, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE.

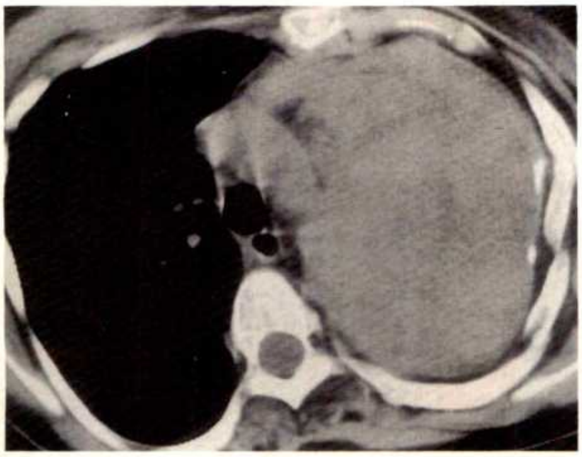


Figure 2. Pre-contrast thoracic CT scan showing a large superior mediastinal mass occupying the whole of the left hemithorax at this level. (The two calcified areas lying lateral to the mass are due to partial volume effect from ribs in the section above.)

left main pulmonary artery. No plane of separation could be identified between the mass and the left lateral aspect of the pericardium. Dilatation of the left internal jugular vein with filling of multiple anterior chest wall collaterals on the left was also noted. Intravenous contrast medium was given at the time of CT scanning and the post-contrast images (Figs 3a and 3b) showed no significant contrast enhancement of any portion of the mass (the mean increase in attenuation value was 17 HU compared with the mean increase in attenuation of chest wall muscles of 25 HU).

Aortography was performed to assess the possibility of embolization to reduce tumour size prior to surgery. This demonstrated an avascular lesion in the superior left hemithorax displacing the major arteries, but did not reveal any feeding vessels (Fig. 4).

In view of the lack of feeding vessels and the likely difficulty of further surgery, it was decided that a course of radiotherapy should be given in an attempt to reduce the tumour size and relieve the symptom of dyspnoea. The patient received a total dose of 4000 cGy to the tumour. When last seen 3 months after therapy, she was less short of breath, although radiologically the size of the mass remained unchanged.

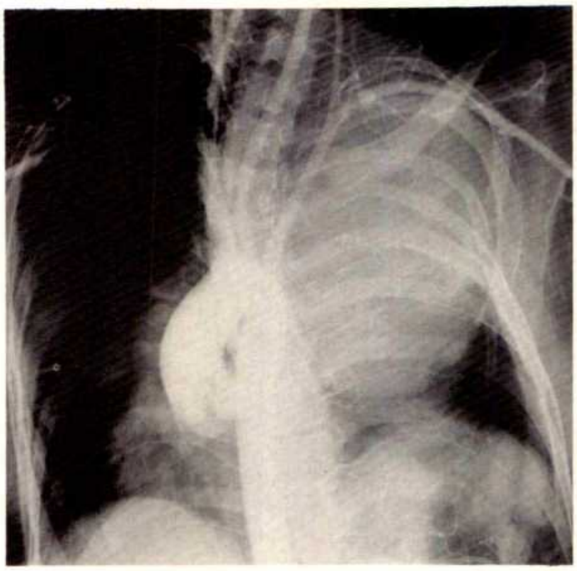
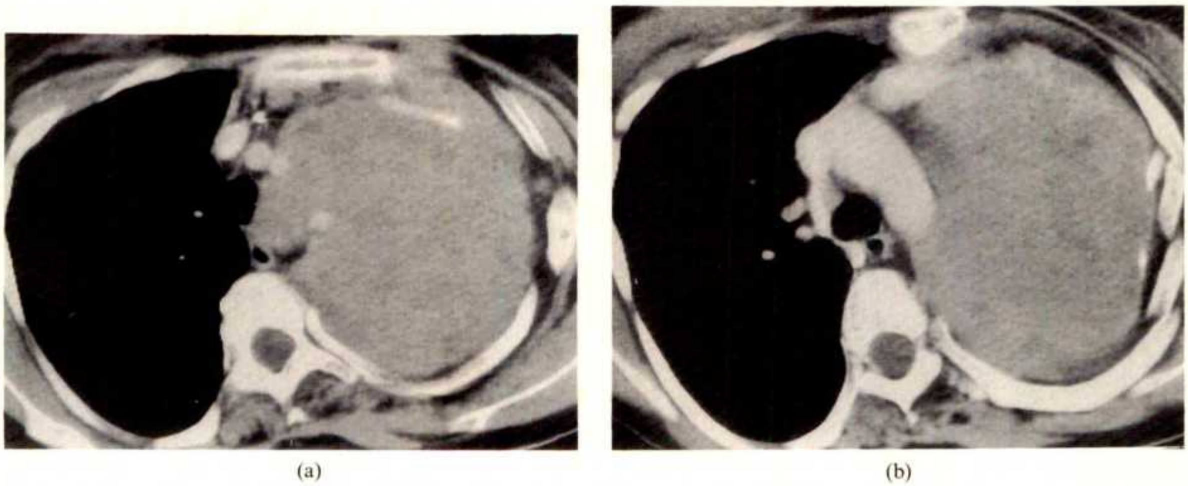


Figure 4. Arch aortogram showing that the aortic arch is pushed down and to the right, with separation of the left common carotid and left subclavian arteries. No abnormal vessels are seen either supplying the mass or ramifying within it.

Discussion

Mediastinal masses due to malformations of vascular or lymphatic origin are unusual. Reports of mediastinal lesions with mixed haemangiomatous and lymph-



(a) (b)

Figure 3. Post-contrast thoracic CT scans (obtained by rapid injection of contrast medium through the left antecubital vein). (a) Note displacement and compression of the left subclavian vein and trachea, and separation of the left common carotid and subclavian arteries by the mass. (b) Comparison with Fig. 2 shows that there has been no significant enhancement of the mass.

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angiomatous elements are particularly rare. We could only find three previously reported cases of lymphangiohaemangioma of the mediastinum. Balbaa and Chesterman (1957) reported the clinical findings and appearances on chest radiography in two cases of lymphangiohaemangioma of the mediastinum, both in very young children (18 months and 7 weeks, respectively). The third reported case described the CT appearances of a lymphangiohaemangioma in a 10-year-old girl (Angtuaco et al, 1983) which showed a near-water density component and contrast enhancement following intravenous contrast medium administration.

It is convenient to divide tumour-like vascular malformations into haemangiomas and lymphangiomas, with a separate sub-division for lymphangiohaemangioma, but recognizing that lymphangiohaemangiomas behave like lymphangiomas (Bruce Williams, 1981; Mulliken & Glowacki, 1982). Lymphangiomas may produce focal masses or they may take a diffuse form. The focal masses are seen in capillary, cavernous and cystic forms. They often contain clear fluid and, therefore, on CT show a density close to that of water (Brown et al, 1986; Pilla et al, 1982). Although lymphangiomas are benign tumours, they may infiltrate along tissue planes and invest vital structures, often making it impossible to remove them completely at surgery with resulting high recurrence rates (Brown et al, 1986). Malignant change has not been reported with lymphangioma or with lymphangiohaemangioma of the mediastinum.

In the only previous report of CT in a case of mediastinal lymphangiohaemangioma, Angtuaco et al (1983) suggested that CT scanning was diagnostically helpful because enhancement of the vascular spaces within the lesion was demonstrated on the post-contrast images. In our case there was no significant difference in attenuation before and after the administration of intravenous contrast medium, despite good opacification of the major intrathoracic arteries and veins. Nor was there any recognizable near-water density component to the lesion. This case illustrates, therefore, that even a large lymphangiohaemangioma may show indeterminate CT attenuation characteristics which do not allow distinction from other soft tissue masses. The lack of contrast enhancement is, however, in keeping with the observation that blood does not always circulate through the vascular elements of a haemangioma, since these structures may be incompletely differentiated (Seybold et al, 1949). In our case, histological examination revealed that the vascular elements were not formed into vessels and it is, therefore, not surprising that neither the CT scan nor the aortogram showed vascularity within the tumour mass.

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Detection of focal nodular hyperplasia with liver colloid single photon emission computed tomography: a case report and review of the literature

By Cumali Aktolun, MD and Hikmet Bayhan, MD

Gülhane Military Medical Academy Hospital, Department of Nuclear Medicine, 06010–Etlik-Ankara, Turkey

(Received April 1990 and in revised form June 1990)

Keywords: Focal nodular hyperplasia, Liver scan, Liver colloid scintigraphy, Liver colloid SPECT, $^{99}\mathrm{Tc}^{m}$-albumin colloid

Focal nodular hyperplasia (FNH) is a benign hamartomatous liver mass (Robbins et al, 1984). It is usually identified incidentally during ultrasonographic examination, other diagnostic procedures or autopsy. The patients are often asymptomatic (Drum, 1982). Physical examination is found to be normal in most of the cases. Jaundice, hepatomegaly, palpable mass, and chronic intermittent vague abdominal pain, especially in the

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Address correspondence to Cumali Aktolun, MD, Gülhane Military Medical Academy Hospital, Department of Nuclear Medicine, 06010-Etlik-Ankara, Turkey.

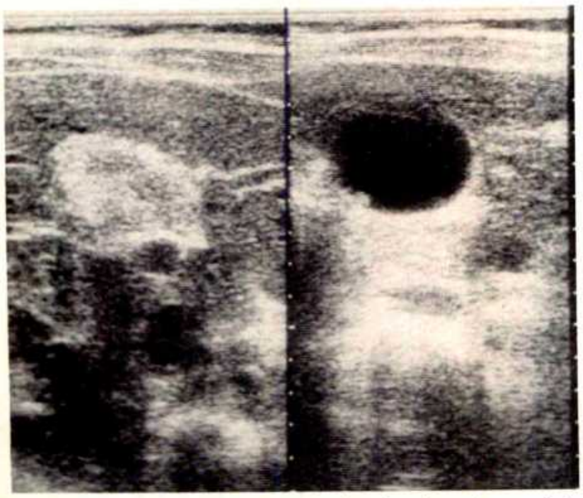


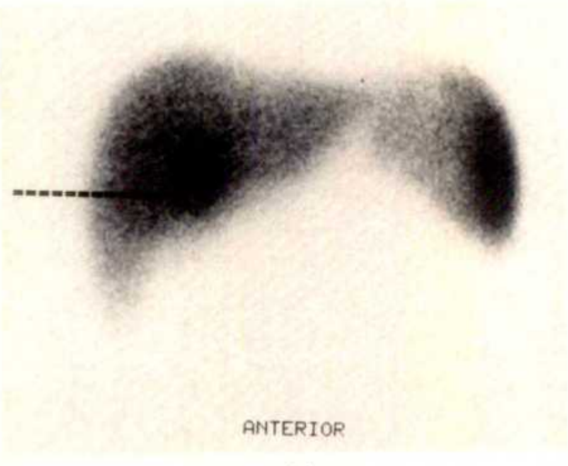
Figure 1. Ultrasonographic examination showing a hyperechoic and well defined space-occupying lesion in the liver (left), and a polyp in the gallbladder (right).

right upper quadrant, may be present in some patients. Eighty-eight per cent of the cases are female, of whom 80% give a history of oral contraceptive or supplemental oestrogen use (Kerlin et al, 1983). The lesion may be solitary (55%) or multiple, and it is usually located in the right lobe of the liver (Rogers et al, 1981), varying in size between 1 and 20 cm, and containing hepatocytes, bile ducts and Kuppfer cells (Rogers et al, 1981; Robbins et al, 1984). Colloid scintigraphic appearance may be hyperactive (40%), hypoactive (30–60%) or normoactive (30–55%) (Diament et al, 1982; Kerlin et al, 1983; Rogers et al, 1981; Welch et al, 1985). A central, stellate-shaped collageneous scar with peripherally radiating septa is the typical histopathologic feature of FNH (Kerlin et al, 1983; Rogers et al, 1981).

We present a case of FNH with planar colloid scintigraphy demonstrating slightly increased uptake in the ultrasonographically detected lesion. Single photon emission computed tomography (SPECT) showed a hyperactive region at the lesion site.

Case report

The patient was a 29-year-old woman, and had a history of oral contraceptive use, pulmonary tuberculosis and jaundice. An ultrasonographic examination was performed to follow up



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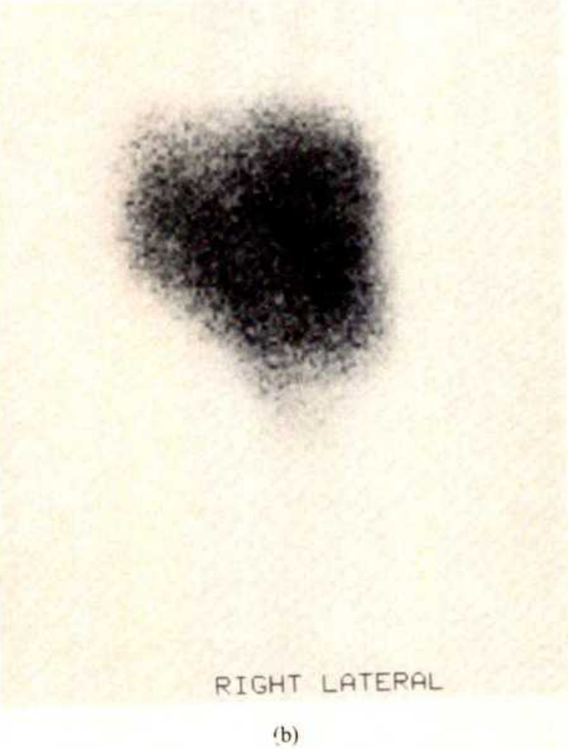

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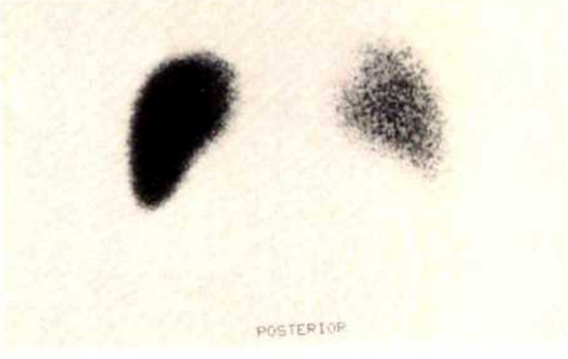

(c)

Figure 2. Focal, slightly increased radiocolloid uptake (arrow) in the liver which could be seen only in the anterior projection (a) of the liver–spleen scintigraphy. Right lateral (b) and posterior (c) projection images appeared normal.

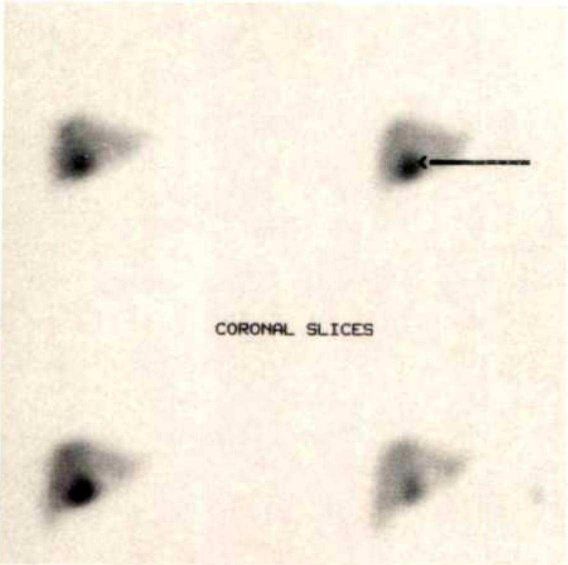

Figure 3. Transaxial, sagittal and coronal slices of SPECT showing a hyperactive region in the liver, most evident in the coronal slices (arrow).

a polyp in the gallbladder diagnosed one year before. A hyperechoic and well defined lesion with an area 55 × 35 mm was detected in the liver in close relation to the gallbladder and porta hepatis (Fig. 1). The differential diagnosis included haemangioma, hepatic cell adenoma, FNH, focal degeneration in the cirrhotic liver and hepatoma.

Hepatic blood pool imaging was carried out with *in vivo* labelled ^{99}Tc^{m} red blood cells to assess the nature of the lesion. The evaluation of dynamic, planar static and SPECT images did not suggest a hepatic haemangioma.

Three days later, the patient was adminstered 222 MBq (6 mCi) ^{99}Tc^{m}-albumin colloid intravenously to evaluate the uptake in the lesion. Seven hundred thousand counts were collected for each of the standard anterior, right lateral and posterior views with a matrix size of 256 × 256. No defect was detected in the planar colloid scintigraphy, but a slightly increased uptake was seen at the site of the ultrasonographically demonstrated lesion in the liver (Fig. 2). A 64 × 64 matrix circular SPECT with 30-second duration 64 frames per 360° was performed just after planar colloid scintigraphy. A hyperactive region (hot spot) was evident in the transaxial, coronal and sagittal slices of SPECT. The lesion was seen most clearly in the coronal slices (Fig. 3). The location of the hyperactive region was coincident with the ultrasonographic appearances. Of the entities listed in the differential diagnosis, only FNH contains reticulo-endothelial cells; other entities would all have been expected to show a defect of uptake at the site of the lesion. Blood pool and colloid imaging were carried out with a GE-400-ACT Starcam gamma camera and computer system.

Coeliac angiography was performed to evaluate the blood supply of the lesion, and no separate artery supply was seen. Histopathologic examination of a sample obtained from ultrasonography-guided needle biopsy revealed the typical structure of FNH.

Discussion

Incidental discovery of an asymptomatic focal hepatic lesion creates a significant diagnostic problem. An integrated approach (ultrasonography, colloid scintigraphy, transmission CT and, in most of the cases, biopsy) is usually necessary for diagnosis; this is especially so for FNH.

Hepatic imaging is a popular application of abdominal SPECT, allowing evaluation of the cross-sectional and three-dimensional distribution of radiocolloid in the liver. It also enhances the contrast resolution. Colloid SPECT has a higher sensitivity and specificity than planar scintigraphy in the detection of hepatic masses (Brendel et al, 1984; Carrasquillo et al, 1983; Strauss et al, 1982).

In conclusion, an ultrasonographically solid hepatic lesion larger than 2 cm in diameter with a scintigraphic finding of high colloid uptake is highly suggestive of FNH, and SPECT can provide further information on the nature of the lesion in addition to a positive contribution to image contrast.

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1991, *The British Journal of Radiology*, *64*, 67–68

Case of the month

Executive distress

By Richard Novell, FRCS, Gerard Stansby, FRCS and Robert Dick, FRCR

Academic Department of Surgery and Department of Radiology, The Royal Free Hospital School of Medicine, London NW3

(Received November 1989 and in revised form February 1990)

A 35-year-old sales executive presented with a history of abdominal discomfort and distention of 2 months duration. Systematic enquiry revealed an increased frequency of bowel action and vague dyspepsia over the same period. Examination revealed a poorly defined mass extending from the periumbilical region to the right iliac fossa. An ultrasound scan of the abdomen demonstrated ascites but was unhelpful in further characterizing the mass. A computed tomographic (CT) scan of the abdomen was then performed (Figs 1 and 2). What does this show and what diagnosis would account for these appearances?

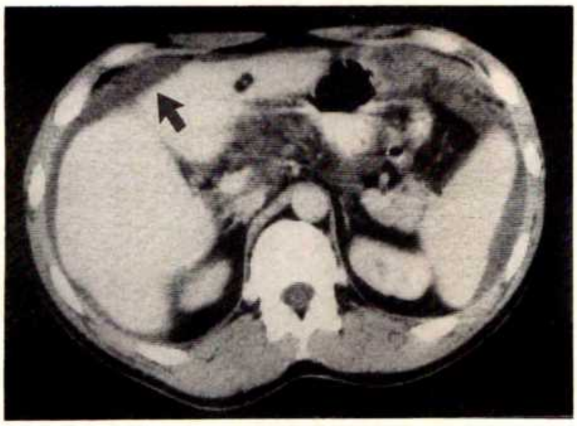

Figure 1. Computed tomographic scan. Arrow shows "scalloping" of the liver edge.

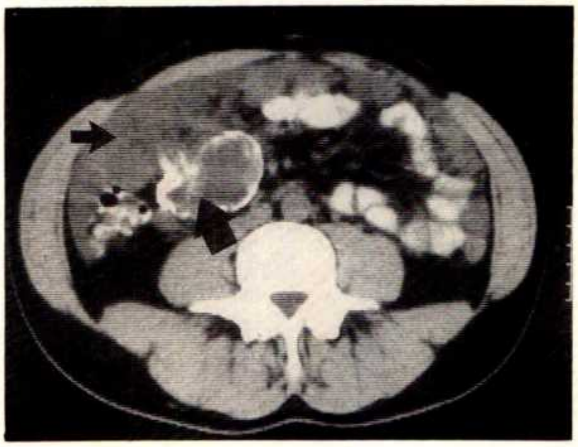

Figure 2. Computed tomographic scan. Small arrow shows soft tissue mass anteriorly, large arrow shows calcified cystic structure posteriorly.

The upper cut of the CT scan, at the level of the lower border of T12, shows a soft tissue mass of low attenuation adjacent to the left lobe of the liver. Indenting or "scalloping" of the liver margin by the mass is seen. On the lower cut, at the level of L4, a rim of soft tissue of similar density to the extrahepatic mass is seen anterior to the small bowel which contains oral contrast material. Posterior to the mass, and continuous with it, is a calcified cystic structure 5 cm in diameter. A large volume of ascites is present.

The patient underwent laparotomy 5 days later. At operation the peritoneal cavity was filled with mucoid ascites. Multiple nodules of tumour extended over the entire visceral and parietal peritoneum. The anterior mass shown on CT proved to be a multiloculated semi-cystic tumour involving the omentum and ascending and transverse colon. Four discrete cystic nodules were present in the mesentery of the terminal ileum. The largest measured 5 cm in diameter and was calcified, corresponding to the CT appearances. An extended right hemicolectomy and omentectomy were performed and the abdomen repeatedly lavaged with distilled water.

Histology revealed a moderately differentiated mucinous adenocarcinoma involving the omentum and serosal peritoneum. No intrinsic abnormality of the ileal, colonic or appendiceal mucosa was found. The mesenteric cysts were found to consist of smooth muscle, lined by columnar epithelium. Three contained mucus and cellular debris only, but the fourth contained invasive adenocarcinoma identical to that in the resected mass. The final diagnosis was pseudomyxoma peritonei in association with mucinous adenocarcinoma arising in an enteric duplication cyst.

The patient was commenced on systemic chemotherapy with mitomycin C and 5-fluorouracil post-operatively; this was later changed to oral chlorambucil. He has returned to work and remains well 21 months following surgery. Repeated ultrasound scans have shown no evidence of recurrent tumour.

Discussion

Ileal duplication cysts are a rare congenital anomaly. They are usually asymptomatic but may be complicated by recurrent abdominal pain, perforation or bleeding, particularly if lined by heterotopic gastric mucosa (Duffy et al, 1974). Intussusception may occur if the cyst is closely associated with the bowel wall, and such cysts tend to present early in life. They are occasionally, as in this case, multiple (Forshall, 1961). Malignant change in a duplication cyst is a very uncommon event (Orr & Edwards, 1975). To our knowledge only three cases of malignancy in ileal cysts have been recorded previously (Smith & Hope, 1985).

Pseudomyxoma peritonei is characterized by massive gelatinous ascites and "studding" of the visceral and parietal peritoneum by mucinous nodules. It most commonly arises from neoplasms of the ovary and appendix (Fernandez & Daly, 1980), although a few cases have been reported to arise from true mucocoele of the appendix. Very uncommonly it may be associated with other adenocarcinomas of gut origin. There has been one previous report of pseudomyxoma in association with heterotopic gastric mucosa from ileal duplication cysts (Duffy et al, 1974). The presentation is characteristically insidious, and the diagnosis most frequently made at operation. Common symptoms are abdominal discomfort and distension, and a mass is often palpable abdominally. Plain abdominal radiographs may show characteristic "eggshell" calcification surrounding encysted mucinous collections. Computed tomography typically demonstrates ascites, low attenuation areas with calcified margins, and displacement or compression of the abdominal viscera. Visceral invasion is not seen (Lee et al, 1986).

Pseudomyxoma spreads exclusively by the trans-coelomic route and appears to have little or no tendency to metastasize to distant sites. The natural history of the disease varies widely and patients may remain relatively asymptomatic for many years, but the eventual prognosis is poor with a 10-year survival of under 20% (Fernandez & Daly, 1980). Surgery is usually palliative, although Sugarbaker et al (1987) report a favourable response to radical surgery combined with intra-peritoneal chemotherapy, with five out of seven patients apparently disease free after 2–4 years.

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Short communication

Broad-beam transmission data in lead for scattered radiation produced at diagnostic energies

By D. J. Rawlings, BSc, MIPSM, K. Faulkner, BSc, MSc, PhD and R. M. Harrison, PhD, FinstP, FIPSM

Regional Medical Physics Department, Newcastle General Hospital, Westgate Road, Newcastle Upon Tyne, NE4 6BE

(*Received March 1990 and in revised form June 1990*)

Keywords: Radiation protection, Broad beam transmission, Diagnostic exposure

The growth of interventional techniques in radiology and the consequent close proximity of staff to patients during screening emphasizes the need for provision of proper protective clothing and for appropriate personnel monitoring for radiological staff. In order to comply fully with the Ionising Radiation Regulations (HMSO, 1985a) and the associated Approved Code of Practice and Guidance Notes (HMSO, 1985b; HMSO, 1988), an employer must demonstrate not only that staff doses are below any relevant limits but also that they are as low as is reasonably practicable. Since heavy protective aprons may be unduly inconvenient to wear and since routine personnel monitoring makes use of just one or two dosemeters, it is important for both the optimization of protective clothing and the estimation of whole body effective dose equivalent (IPSM, 1977) that the broad beam shielding properties of lead under relevant working conditions are known (Faulkner & Harrison, 1988).

Although there are several sources which tabulate the broad beam shielding characteristics of lead and other materials at diagnostic X-ray energies (BSI, 1971; HMSO, 1971; O'Riordan & Brotherton, 1968; Binks, 1943; NCRP, 1976), a number of limitations exist when these data are applied in practice to lead apron shielding:

(1) the data represent primary beam attenuation whereas personnel need to be protected against scatter;
(2) data for only a limited number of tube voltages are represented possibly leading to difficult interpolation;
(3) a very large range of thicknesses is covered by the data and accuracy may be compromised at the low lead equivalent thicknesses of aprons.

In this paper, measurements of broad beam attenuation of scatter in lead rubber aprons under realistic conditions are described, and the results compared with existing primary beam data.

Experimental arrangement

A wax phantom (60 × 30 × 23 cm) was placed on an X-ray table and irradiated with a vertical X-ray beam of field size 27 × 17 cm^2 and a source to surface distance of 50 cm. This was taken to represent a patient undergoing a routine interventional procedure, for example in a coronary care ward or in a specialist radiographic facility. The X-ray apparatus consisted of a Medio DLX X-ray set with a Machlett Dynamax tube and a 16° tungsten target. A fully rectified unsmoothed voltage waveform was used with generating voltages in the range 50–120 kVp. The voltage waveform was similar to those provided by generators of mobile image intensifier TV systems commonly found in coronary care units. Tube voltages were checked using a Keithley non-invasive divider which had a calibration traceable to primary standards. A 1.8 litre ion chamber, connected to a digital electrometer (MDH) was placed close to the phantom but outside the primary beam so that it detected radiation scattered through approximately 90° (see Fig. 1). Specifications for the chamber and electrometer indicated a measurement resolution of 0.01 μGy repeatable to within 1%. The energy response of the chamber, over the range of qualities encountered, was uniform to within 1%. The chamber, protected from X-ray tube leakage by 6 mm lead shielding, was positioned with its centre 13 cm from the nearest face of the phantom. The radiation striking the chamber was taken to represent that incident on a member or staff attending the patient. A series of large lead sheets 500 × 500 × 0.15 mm

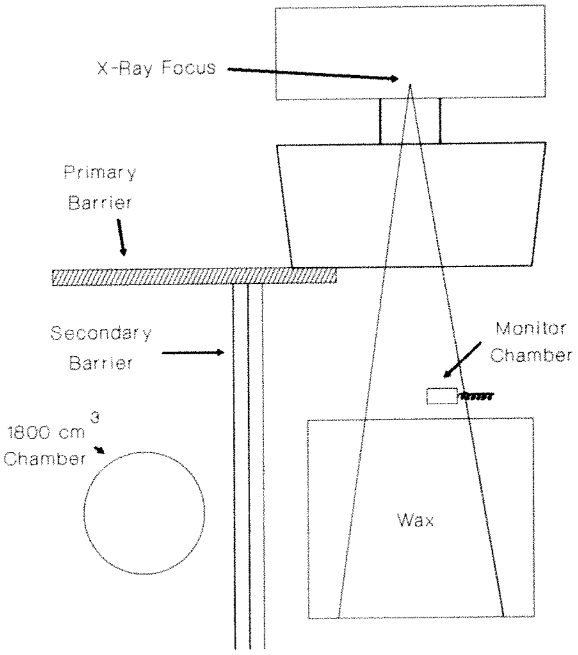

Figure 1. Apparatus for measurement of broad beam shielding characteristics of scatter from a wax phantom irradiated by diagnostic X rays.

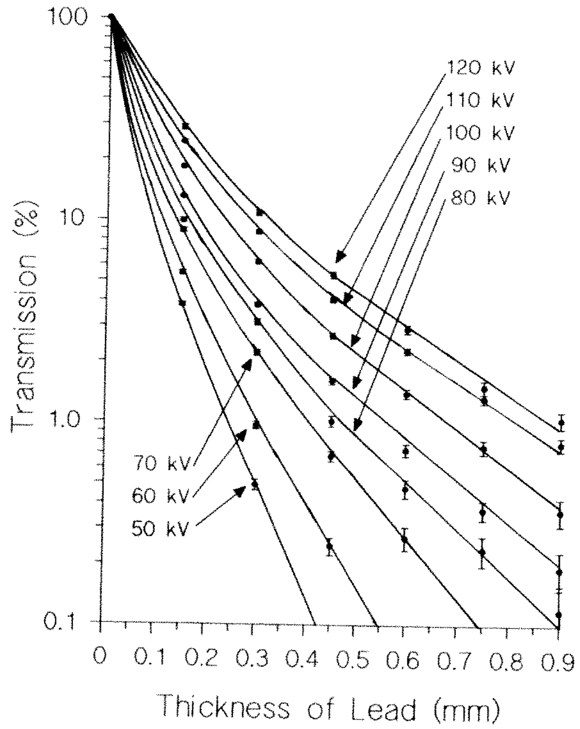

Figure 2. Scatter transmission characteristics.

was placed in the 6 cm gap between scatterer and detector, and the transmitted radiation dose was measured at different thicknesses of lead. A small correction was made for the residual scatter from the walls and floor of the room. This was assessed separately at each generating voltage by placing a thick shield (3.4 mm lead) between scatterer and detector. A further ion chamber, connected to an analogue electrometer and stable to within 2%, was placed in the primary beam to act as a monitor.

Results

The results shown in Fig. 2 may be compared with primary beam data (HMSO, 1971) over a limited number of generating voltages. Although there was generally good agreement, it was found that at the highest generating voltages, the scatter data indicated significantly greater penetration than the recommended primary beam data. According to the measured data, an apron of 0.25 mm lead equivalent thickness would transmit 15% of the broad beam scatter at a generating potential of 120 kVp, whereas at the same thickness only approximately 10% of the primary beam would be transmitted under broad beam conditions. Transmission data for common lead apron thicknesses are shown in Table I.

Discussion

Although the maximum energy of the scattered radiation is less than that of the primary beam, beam hardening acts to increase the quality of the radiation beam within the patient (Birch et al, 1979). Depth dose characteristics over the diagnostic range of energies (for example, Wall et al, 1988) indicate that significant beam hardening generally occurs within about 5 cm of the surface but that beyond this depth there is little change in beam quality. It would appear therefore that the observed results may be consistent with the effects of beam hardening of both primary and secondary radiation within the patient.

Table I. Broad beam transmission of 90° scatter by lead aprons as a percentage of unshielded dose

Generating voltage (kVp)	0.25 mm Pb apron(%)	0.35 mm Pb apron(%)
50	0.92	0.23
60	1.7	0.62
70	3.3	1.5
80	4.4	2.1
90	5.8	2.8
100	8.6	4.6
110	12	6.6
120	15	8.6

Keane and Spiegler (1951) measured first half value layer data from radiation scattered from deep within a phantom and, consistent with the current results, found values to be higher than those of the primary beam. However, Trout and Kelley (1972) measured attenuation data over a similar quality range and generally found primary beam quality to be greatest, in contrast to the present result. However a field size of 900 cm² at the phantom surface is specified. This is much larger than that typically found in practice. In addition, the volume of the ionization chamber and the size of the lead attenuators are not specified and so a direct comparison with the current work may not be appropriate.

The data shown in Fig. 2 are appropriate for use in optimizing protection or estimating whole body effective dose equivalent to a member of staff carrying out duties close to a patient during screening procedures (Faulkner & Harrison, 1988). The data are tabulated for a range of generating voltages and lead equivalences which are relevant for these purposes. Since beam hardening takes place whenever radiation is scattered from deep within a patient it is apparent that any member of staff required to wear a lead apron may be subject to beam hardened scatter, except where the scattering volume is very small or there is otherwise a large proportion of superficial scatter. Since only 5 cm of tissue would normally be required for complete beam hardening, it is also apparent that under most circumstances the spectrum of scattered radiation could not be expected to be strongly dependent upon field size.

The attenuation data presented here are therefore generally applicable whenever radiation, scattered laterally from a patient undergoing a diagnostic procedure, is considered. Overall uncertainty in the data is indicated by the error bars in Fig. 2, and may be attributed to small variations in the X-ray generating potential and uncertainties in the residual scatter from sources other than the phantom. This may be contrasted with the uncertainty associated with the interpretation of data from existing primary sources, limited by the large range of lead equivalences, and small number of beam qualities represented.

The data in Table I may be used as a guide to the scatter transmission characteristics of commonly used lead aprons. This data emphasizes the need for the specification of lead apron thickness dependent on the tube potential range used clinically, and is in accordance with the advice given in paragraph 3.70 of the Guidance Notes (HMSO, 1988). If the advice in the guidance notes is followed, then it may be deduced from the data presented in Table I that the scatter transmission through body lead aprons will be less than 10%.

Acknowledgments

The authors would like to thank Professor K. Boddy for his continued support and encouragement, and Messrs K. Robson and N. Marshall for assistance with the graphics.

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1991, *The British Journal of Radiology*, *64*, 72–74

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Bilateral pneumothorax as a presenting feature of metastatic angiosarcoma of the scalp

The Editor—Sir,

Lawton et al (1990) observe that metastatic angiosarcoma is a rare condition and is associated with extremely poor survival following the development of lung complications. They also state that, although radical doses of radiotherapy (44–60 Gy over 4–6 weeks, respectively, 4 fractions per week) have been followed by long term control of local disease, this may not necessarily correlate with improved survival. A further case, identified by retrospective review of patients' records of the Skin Unit of the Peter MacCallum Cancer Institute (PMCI) in Melbourne, is described here to report the response to hypofractionated treatment.

An 81-year-old woman presented to her GP with a 4-month history of a "blood blister" on the right forehead, initially 2 cm in diameter, which had rapidly increased in size to 8 × 5 × 3 cm. Following surgical referral, the lesion was completely excised and the defect grafted. One month post-operatively, however, an extensive area of induration and pigmentation was noted arising from the inferior aspect of the surgical site. A diagnosis of recurrent disease was confirmed and the patient referred to the PMCI for radiotherapy.

Treatment was prescribed with superficial radiotherapy using a 70 × 70 mm field to cover the clinically determined extent of disease and giving 30 Gy skin dose in 3 fractions at 1/week. Treatment was well tolerated and a complete response was documented on clinical examination 2 months after completion of superficial radiotherapy.

However, a further 4 months later, the patient complained of haemoptysis, and a chest radiograph was reported as showing multiple opacities in both lungs consistent with metastatic disease. Megavoltage irradiation was given to the mediastinum and adjacent lungfields using anterior and posterior parallel opposed fields, giving 12 Gy maximum permissible dose in 3 fractions in 1 week. The haemoptysis settled after the first fraction and a repeat chest radiograph on subsequent follow-up showed the persistence of only one nodule in the left lower bone, outside the treatment field.

The patient remained asymptomatic for the following 9 months, when she again complained of haemoptysis. There was no clinical evidence of active disease at the primary site. Chest radiography showed progressive disease with widespread nodules, and despite further palliative megavoltage therapy, the patient's condition deteriorated rapidly and she died 2 months later. Post-mortem examination was not performed.

Sarcomas are generally regarded as relatively unresponsive to radiation and it has been proposed that, if this is because of the presence of a large shoulder on the cell survival curve, then using fewer large fractions (hypofractionation) might be expected to improve response. However, large dose fractions increase late normal tissue damage which is of great importance in radical treatment. This was noted in 23 out of 32 evaluable patients in the study by Ashby et al (1986), who reported no apparent improvement in therapeutic gain for large weekly fractions.

In the case presented here, owing to the aggressive nature of the disease, with short presenting history and time of first recurrence, the initial radiotherapy was given only with palliative intent. A complete remission was noted, however, and although metastases developed, there was no evidence of further active disease at the primary site. Similarly, after a short course of megavoltage therapy to the chest, at least a partial response was seen initially and palliation of symptoms was successful, although local control of disease was not gained.

This report illustrates that short courses of large dose fractions may be sufficient to achieve treatment objectives in the management of locally advanced and metastatic angiosarcoma.

Yours, etc.
Bruce Sizer

Essex County Hospital,
Lexden Road,
Colchester,
Essex, UK

(*Received July 1990*)

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Retroperitoneal haematoma and pelvic haematoma following orchidectomy

The Editor—Sir,

We read with interest the papers by Page et al (1990) and Russell et al (1990) on the importance of differentiating retroperitoneal haematoma following transinguinal

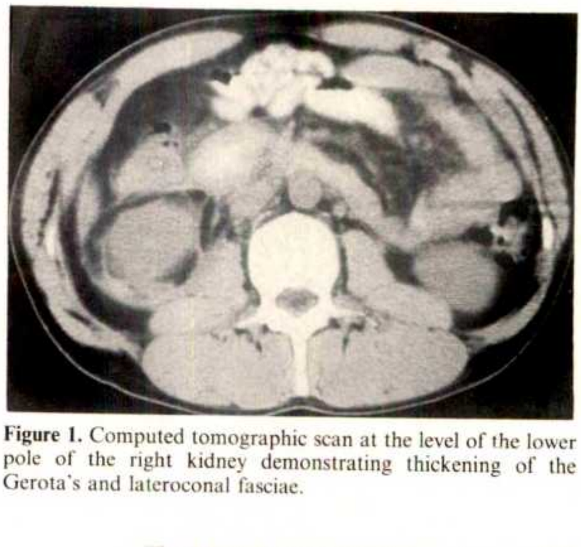

Figure 1. Computed tomographic scan at the level of the lower pole of the right kidney demonstrating thickening of the Gerota's and lateroconal fasciae.

orchidectomy from metastatic lymph node involvement. We have recently seen a 24-year-old man who underwent a right inguinal orchidectomy for testicular swelling of 3 months duration. Histological examination of the resected testis showed malignant teratoma undifferentiated (MTU), with no evidence of vascular invasion and absence of yolk sac elements. Tumour markers were negative pre-operatively and have remained so. A staging computed tomogram (CT) performed 7 days post-operatively demonstrated an 8 cm high attenuation mass in the right side of the pelvis extending superiorly to the lower pole of the right kidney. In addition there was marked thickening of the lateroconal and Gerota's fasciae, increased attenuation of the perirenal fat and loss of the normal fat planes around the inferior vena cava (Fig. 1). This finding indicated the inflammatory nature of the lesion and prompted the correct diagnosis. The haemoglobin was then noted to have fallen to 10.3 g/dl. Four weeks post-orchidectomy the patient is well. No antitumour therapy is planned.

We find it surprising that in the six reported cases there was no mention of a similar appearance. The presence of inflammation in conjunction with the characteristic CT appearances of retroperitoneal haematoma (Jeffery, 1983) should enable the correct diagnosis to be made.

Yours, etc.
C. Kennedy
*S. Harland
*G. Watson
*C. Parker

Department of Imaging,
The Middlesex Hospital,
Mortimer Street,
London W1N 8AA and
*The London Institute of Urology,
London WC2H 8JE

(Received July 1990)

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The physical dimensions of the compressed breast

The Editor—Sir,

The success of the National Breast Screening Program relies on accurate dose measurements, essential for any risk–benefit analysis and radiation protection considerations (Forrest, 1986). This need to measure absorbed doses within and around the irradiated breast necessitates the use of carefully selected materials from which phantoms and radiation detectors can be constructed. In addition, the relevancy of the geometry and physical dimensions of anthropomorphic phantoms is paramount. Breast phantoms for image quality and dosimetry should be pertinent to the breast which has been compressed for examination, similarly tissue substitutes used in the phantom must have either known elemental composition and mass densities or known radiation absorption and scattering properties for the relevant type and energy of radiation used in mammography (ICRU, 1989).

Table I. Results of the Compressed Breast Size Study

	Age (years)	Thickness (cm)	Width (cm)	Breadth (cm)
Mean	48.5	5.2	18	8.1
Standard deviation	9.1	1.1	2.4	2.1
Maximum value	82	8.6	25	17.4
Minimum value	31	2.5	12	1.4

To this end a study has been carried out to find an average compressed breast size.

The study was not meant to increase the patient examination time and certainly not prolong the time the breast was under compression. Mammographers filled in a form with data on thickness, width and breadth of each breast, exposure factors and the age of the individual. The thickness of the compressed breast was read off a scale on the mammography unit. The other measurements of width of breast and distance from the nipple to the chest wall were recorded from the mammographs. These dimensions have been called thickness, width and breadth. These terms are clarified in Fig. 1.

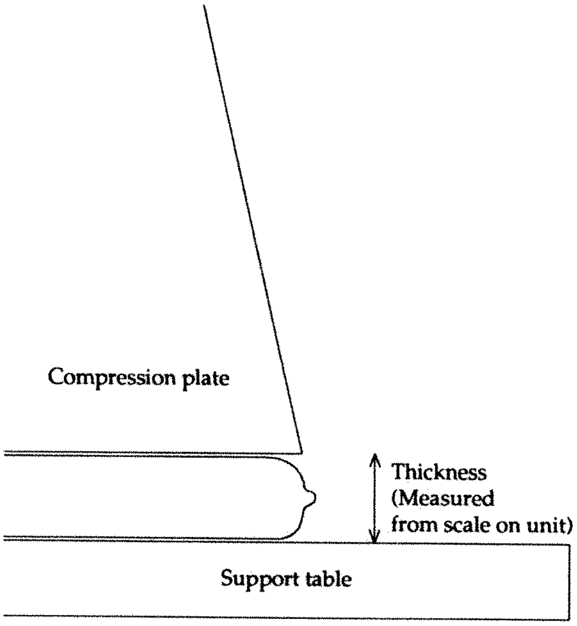
The results of this study are from 216 different compressed breasts and are shown in Table I.

The compressed breast size study has given an average thickness under compression of 5.2 ± 1.1 cm with a range in thicknesses of 2.5 cm to 8.6 cm.

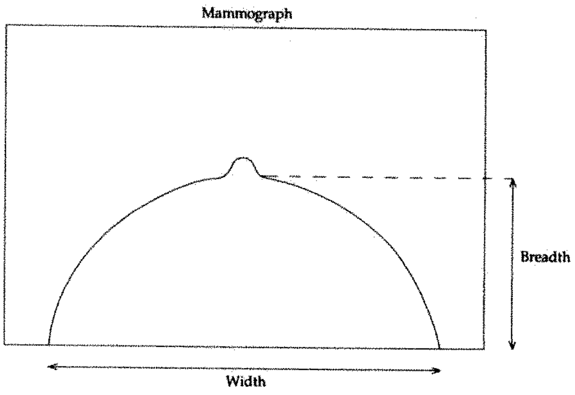
Several authors have calculated optimum X-ray energies for mammography using, as a criterion, the maximum signal-to-noise ratio obtainable per unit absorbed dose to the breast (Beaman & Lillicrap, 1982).

The predicted optimum X-ray energy increases with breast thickness. However, increasing the generator voltage has little effect on the spectrum from a molybdenum target (Marshall et al, 1975). This average thickness of 5.2 cm suggests improved image quality with optimum spectra from a filtered tungsten target as opposed to a molybdenum target molybdenum filter combination (Beaman & Lillicrap, 1982). However, the NHS Procurement Directorate has already stipulated that the target material of mammography units in Breast Screening and Assessment Centres should be molybdenum (DHSS, 1987). The dimensions of the study are also up to 3 cm thicker than some of the available breast phantoms on the market today.

A factor which affects the measured compressed breast size is the mammographic technique itself. Breast Screening Centres may not yet be uniform in their application of compression, and it is important to record widths and breadths from the mammographs along with thicknesses. When width and breadth measurements from one centre are comparable to another centre yet the thicknesses are smaller, it may be inferred that the latter centre is applying firmer compression than the former. If a centre presents with all dimensions being larger than the norm then that centre may well be examining a sample from a population of larger than normal breasts. It is



(a)



(b)

Figure 1. Diagram showing thickness, width and breadth measurements.

hoped that such dimensions be recorded routinely throughout the country to establish compressed breast dimensions.

Yours, etc.,
I. Fife

The Radiation Physics Department,
St Bartholomew's Hospital London,
West Smithfield,
London EC1A 7BE

(*Received August 1990*)

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1991, *The British Journal of Radiology*, *64*, 75–80

Proceedings of the British Institute of Radiology

Current progress in magnetic resonance imaging: scientific and clinical developments in the UK

Abstracts of papers presented at an all day meeting organized by the BIR for the Diagnostic Methods Committee held at the Edward Lewis Lecture Theatre, Windeyer Building, Middlesex Hospital, Mortimer Street, London W1N 8AA on Monday 15 October 1990

This meeting was generously sponsored by Premise Engineering Ltd and Schering Health Care

Introduction, by B. S. Worthington
A novel approach to quantitative flow measurements, by M. Tarnawski, D. A. Porter, M. J. Graves, T. S. Padayachee, M. G. Taylor and M. A. Smith
In vivo proton electron double resonance imaging of nitroxide free radicals in the rat, by I. Nicholson, D. J. Lurie, M. A. Foster and J. R. Malard
Measurement of blood–brain barrier permeablility and leakage space using dynamic Gd-DTPA MRI scanning, by P. Tofts and A. Kermode
High resolution *in vivo* MRI of healthy cartilage, by T. A. Carpenter, L. D. Hall and R. J. Hodgson
The use of a diffusion-weighted pulse sequence to suppress the signal from extracellular fluid in MRI of a rabbit knee model of inflammatory arthritis, by D. Checkley, J. C. Waterton and D. Johnstone
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Combined MRI and localized ^{1}H NMR spectropcopy of the brain in children, by S. Austin, A. Connelly and D. Gadian

Introduction

B. S. Worthington
Queen's Medical Centre, Nottingham

In both 1986 and 1989, multidisciplinary meetings were held under the auspices of the British Institute of Radiology for those actively engaged in magnetic resonance as applied to medicine. These one-day meetings were extremely successful, providing an environment for a valuable scientific interchange between participants, and it was decided that a similar meeting should be held in 1990.

During the first part of the meeting, a group of speakers (Dr I. Young, Prof. G. Bydder, Prof. B. S .Worthington, Prof. I. Isherwood and Dr J. Griffiths) gave brief overviews of what they raegarded as being the most significant develpments during the past year within their respective areas of interest. Topics covered included improvements in coil design and the development of internal surface coils such as those used in imaging the postate and cervix; the further extension and refinement of MR angiography; the new imaging parameters represented in translational diffusion and magnetization transfer contrast; further developments in contrast agents and fast imaging techniques with a discussion of their contribution to improvements in abdominal imaging, and also how both MR imaging and spectroscopy were contributing the evaluation of the pathophysiology of several diseases and being used to monitor the effect of different therapeutic regimes. The remainder, and larger part of the meeting, consisted of short proffered presentations, the abstracts of which follow.

A novel approach to quantitative flow measurements

M. Tarnawski, D. A. Porter, M. J. Graves, T. S. Padayachee, M. G. Taylor and M. A. Smith
Division of Radiological Sciences, UMDS, Guy's Hospital, London

Magnetic resonance measurements of flow commonly use phase contrast sequences to obtain images where the vessel cross-sectional area can be measured. The pixel values within the vessel are proportional to the velocity within the image pixel, thus the average vessel velocity can be calculated. Combining the area and average velocity then yields the flow. This method is limited because of the poor resolution of MRI, thus is used for larger vessels. For small vessels the inaccurate measurement of area influences the calculated flow, *e. g.* a 10% error in diameter gives a 20% error in flow. A theoretical analysis of the partial volume effect shows that the product of the pixel velocity and area is approximately equal to the flow in the part of the vessel contained within the pixel. Extension of this analysis to a region of interest (ROI) larger than the vessel means that the area does not need to be measured. Hence flow measurements in small diameter vessels are possible. The ROI flow method was verified with phantom experiments and applied *in vivo* for the measurement of flow in the middle cerebral artery in volunteers.

In vivo proton electron double resonance imaging of nitroxide free radicals in the rat

I. Nicholson, D. J. Lurie, M. A. Foster and J. R. Mallard
Department of Bio-Medical Physics and Bio-Engineering University of Aberdeen, Foresterhill, Aberdeen AB9 2ZD

Proton electron double resonance imaging (PEDRI) is a new technique for imaging free radicals in aqueous samples. Conventional NMR images are collected whilst irradiating the EPR resonance of a free radical in solution. This enhances the NMR signal in regions where the free radical influences proton relaxation. We have imaged the distribution of the nitroxide free radical 3-carboxy-proxyl (PCA) following intravenous administration to adult Sprague Dawley rats. The EPR resonance was irradiated at 238 MHz using an Alderman–Grant coil placed around the solenoidal NMR coil operating at 425 KHz. The EPR irradiation was pulsed for alternate signal collections allowing images with and without EPR irradiation to be collected simultaneously and a difference image calculated showing only areas of enhancement, *i.e.* free radical concentration. Images were collected on a 32 x 32 matrix with repetition time 500 ms and 7.5 cm field of view. The free radical appeared in the liver and kidneys in the image collected immediately after injection of PCA. Subsequent clearance of the free radical was observed over a period of 30 minutes and time curves of the clearance plotted over regions of interest obtained from the image series.

Measurement of blood–brain barrier permeability and leakage space using duynamic Gd-DTPA MRI scanning

Paul Tofts and Allan Kermode
Institute of Neurology, Queen Square, London

Alteration of signal after injection of Gd-DTPA is recognized as being the most appropriate way to detect blood-brain-barrier breakdown. Although most imaging has been non-quantitative (simply looking for the presence or absence of enhancement), two quantitative parameters are available provided the appropriate imaging procedure is used. By imaging continuously after injection, the time course of signal alteration can be followed. A pharmacokinetic model predicts model curves. Fitting these to the measured ones allows the permeability surface area product per unit volume (k) and the leakage space per unit volume (v_l) to be estimated. Inter-arterial sampling is avoided by using published plasma concentration *versus* time curves. Typical values in acute Multiple Sclerosis are k = 0.01–0.05/minute, v_l = 21–49%. The former suggest permeability in the range 4–17.10^{-6} cm/sec, close the values measured in muscle by traditional means; the latter are close to values for extracellular space in MS, as measured by biexponential analysis of transverse magnetisation decay curves, and strongly suggest that Gd-DTPA leaks into the extracellular space.

High resolution *in vivo* MRI of healthy cartilage

T.A. Carpenter, L.D. Hall and R.J. Hodgson
Cambridge

MRI is already established as a useful clinical tool for the evaluation of cartilage extent. The object of this research is to extend this to investigate structure within the cartilage, with a view to developing imaging techniques useful for the assessment of the early stages of cartilage degenerative diseases. Experiments were performed on the distal interphalangeal joints of normal, healthy volunteers in a 30 cm horizontal bore 2 Tesla magnet. Variable echo time, 1331 chemical shift selective spin echo pulse sequences were used which, with probes and gradients developed in house, provided 0.12 mm in-plane resolution from a 1.8 mm sagittal slice. Images revealed a hypo-intense region at the surface of the cartilage, not as a result of susceptibility artefacts. Variable echo time experiments suggested the free water content was lower in this region.

The use of a diffusion-weighted pulse sequence to suppress the signal from extracellular fluid in MRI of a rabbit knee model of inflammatory arthritis

D. Checkley, J. C. Waterton and D. Johnstone
Chemistry 1 and Bioscience 1 Departments, ICI Pharmaceuticals, Alderley Park, Macclesfield, Cheshire SK10 4TG

A rabbit model of inflammatory arthritis, which has similarities to human rheumatoid arthritis, has previously been employed to assist drug discovery. The inflammatory process in the model is seen as high-signal areas in T_2-weighted images. In order to isolate the tissue component (pannus) of this inflammatory process, it is necessary to suppress the signal from extracellular fluid. To achieve this, we acquired a heavily diffusion-weighted stimulated-echo image and, simultaneously, a normal TE36 spin echo image. The freely diffusing extracellular fluid signal was preferentially suppressed compared with the more slowly diffusing signal associated with the inflammatory cells. Results were displayed as a pixel-by-pixel calculated ratio of the stimulated echo to the spin-echo image: this approximates to an apparent diffusion-coefficient map. This approach has allowed the quantification of the two components of the inflammatory process (tissue and fluid) and may be of value in the development of novel disease-modifying anti-rheumatic drugs.

Diffusion-weighted imaging in the study of kinicacid lesions in the rat brain

N. Van Bruggen, *M. K. King, *R. Ahier, *J. E. Cremer, †J. V. Hajnal, S. R. Williams, †M. Doran and D. G. Gadian
*Hunterian Institute, Royal College of Surgeons, London and *MRC Cyclotron Unit and †NMR Unit, Hammersmith Hospital, London*

Contrast in magnetic resonance images can be generated by a wide variety of mechanisms. Recently, it has been shown that diffusion-weighted imaging (DWI) can reveal certain structures and pathologies in the brain more clearly than conventional imaging sequences. For example, in studies of regional cerebral ischaemia in cats, it has been shown that DWI can detect early occlusive brain injury not obvious from conventional T_2-weighted images. Furthermore, it has been reported that the anisotropic nature of the diffusion of water in white matter may be used to visualize tracts in the cat brain. Clinical images have recently been obtained which are consistent with these observations. Preliminary data comparing T_2-weighted and diffusion-weighted imaging to monitor kainic acid lesions in the rat brain will be presented. Our observations show improved image contrast between oedematous lesions and the unaffected regions using DWI. Furthermore, we show how the anisotropically restricted diffusion of water associated with white matter can be used to highlight white matter tracts and to provide information concerning their orientation in the rat brain.

MRI of anisotropically restricted diffusion in the nervous system

Mark Doran, Joseph Hajnal, Graeme Bydder and Ian Young
London

The Stejskal and Tanner pulsed gradient sequence can be used to introduce diffusion-weighted contrast into the spin echo sequence. The amplitude images have two interesting properties: anisotropic directional contrast and increased sensitivity, particularly to acute pathological changes. The anisotropically directional contrast probably arises from restricted mobility of water within the axon. It is suspected that the myelin sheath acts as a hydrophobic barrier to water. Mobility is reduced in directions across the length of the axon and unrestriced along it giving white matter either a high or low signal , respectively, on very T_2-weighted images. This allows specific white matter tracts to be highlighted. Application of these sequences to a variety of pathologies has revealed increased sensitivity to a variety of pathologies. Novel features of normal anatomy are discernable. ARDI allows specific tracts to be examined with side to side differences being assesssed in epilipsy. Lesions in multiple sclerosis are more extensive than with standard spin echo's. Imaging of neonates demonstrates the directional development of myelin and provides greater contrast than the inversion recovery sequence.

Regional myocardial contractile function during pharmacological stress: studies with dipyridamole and dobutamine n coronary artery disease

D. J. Pennell, S. R. Underwood, C. C. Manzara, P. J. Ell, R. H. Swanton, J. M. Walker, D. B. Longmore
Magnetic ResonanceUnit, National Heart and Chest Hospitals, London, Institute of Nuclear Medicine, UCMSM, London and Department of Cardiology, Middlesex Hospital, London

Objectives. Exercise stress testing in the magnetic resonance scanner is difficult because of space restriction and unacceptable movement artefact. We have assessed the use of pharmacological stress as an alternative for the detection of coronary artery disease. *Methods.* Patients admitted for coronary angiography were recruited. Cine imaging was performed in the horizontal and vertical long axes and short axis of the heart. Without removing the patient from the magnet, either dipyridamole (0.56 mg/kg) or dobutamine (5–20 μg/kg/min) was infused intravenously and imaging repeated. Wall motion was graded normal, hypokinetic or akinetic in nine myocardial segments and a new wall motion abnormality defined as a reduction of at least one grade between baseline and stress. All patients also underwent thallium myocardial perfusion imaging using dipyridamole or dobutamine as appropriate. *Results.* Of 40 patients studied with dipyridamole, 39 had coronary artery disease, 36 had reversible myocardial ischaemia by thallium imaging and 24 (67%) had dipyridamole-induced wall motion abnormalities detected by magnetic resonance imaging. Of 25 patients studied with dobutamine, 22 had coronary artery disease, 21 had reversible myocardial ischaemia by thallium imaging and 20 (95%) had dobutamine induced wall motion abnormalities detected by magnetic resonance imaging. In both studies there was a close correlation between the perfusion defect and the wall motion abnormality. *Conclusion.* Magnetic resonance imaging during pharmacological stress is feasible and well tolerated. Coronary artery disease is detectable as reversible regional wall motion abnormalities. Dobutamine is superior to dipyridamole for producing reversible myocardial ischaemia which results from its action a B-agonist as opposed to a coronary vasodilator.

Short echo time MR jet velocity mapping assessed *in vitro* and applied in aortic coarctation and ventriculopulmonary conduit obstruction

Philip Kilner, David Firmin, Carla Manzara, Raad Mohiaddin, Richard Underwood, Simon Rees and Donald Longmore
The Magnetic Resonance Unit of The National Heart and Chest Hospitals, London

Purpose: To assess short echo time magnetic resonance jet velocity mapping as a means of measuring post stenotic jet velocities *in vitro* and in patients. *Materials and methods.* Magnetic resonance jet velocity mapping was performed, using a Picker 0.5 Tesla machine and the field even-echo rephasing sequence with a 3.6 ms echo time, in stenotic flow phantoms and in 50 patients (mean age 31, range 12–72) with aortic coarctation ($n = 27$) and stenoses of valved conduits ($n = 23$). Where possible, results were compared with those available from Doppler ultrasound and catheter studies. *Results*: Magnetic resonance velocity maps clearly demonstrated the shape and location of jets, and velocity measurements correlated well with Doppler measurements up to 6 m/s *in vitro* ($r = 0.996$). In patients, jet velocities up to 5.5 m/s were mapped, and for 21 cases in which comparison was possible, agreement with Doppler was good: mean of peak velocity measurements was 2.7 m/s, mean of differences (SD of differences), 0.05 m/s (+0.2 m/s). Unclear velocity maps were attributed to slight misplacement of the image plane in nine cases. *Conclusion*: Short echo magnetic resonace velocity mapping is likely to have considerable importance as a non-invasive means for locating and evaluating stenoses, particularly at sites inaccessible to ultrasound.

Three-dimensional gradient echo MRI of the knee: comparison with artroscipy in 100 patients

C.W. Heron and P.T. Calvert
Departments of Radiology and Orthopaedic Surgery, St George's Hospital, Blackshaw Road, London SW17 0QT

This prospective study was undertaken in order to compare the results of three-dimensional gradient echo MRI of the knee with the findings at arthroscopy. The MRI examinations were performed using a Siemen's Magneton operating at 1.5 Tesla. Three-dimensional gradient echo images were obtained in both the sagittal and coronal planes using the pulse sequence known as FISP. Menisci were classified as normal, degenerate or torn. There was very high correlation between the two examinations in the detection of tears but MRI detected more degenerate menisci than were seen at arthroscopy. Anterior and posterior cruciate ligaments were categorised as normal, partially torn or completely torn. The correlation between the two examinations was slightly lower than in the detection of meniscal abnormalities. Degenerative changes in hyaline cartilage were graded according to severity. Magnetic resonance imaging was accurate in detecting later stages of degeneration when loss of hyaline cartilage was present, but failed to detect minor fissuring in some cases. In conclusion, three dimensional gradient echo imaging currently enables a full data set to be acquired in approximately 5 minutes and allows accurate assessment of the menisci, ligaments and hyaline cartilage.

The early assessment of acute spinal injuries using a 0.2 T permanent magnet system

P. Savage and R. Bodley
Stoke Manderville Hospital, Buckinghamshire

The aim was to assess the possible role of MRI in the early investigation (*i.e.* within 48 hours if possible) of patients with traumatic spinal injury. All patients admitted to the National Spinal Injuries Centre, Stoke Mandeville Hospital between July and October 1990 were assessed as soon after arrival as was medically possible. The examinations were carried out on Hitachi permanent magnet MRI system which operates at a field strength of 0.2 T. In many cases a modified Stryker Frame was used to facilitate patient handling. The relevant spinal segment in all the patients was examined in the saittal plane with a 5 mm slice thickness employing both T_1- and T_2-weighted spin-echo sequences. Axial cuts were taken if appropriate and several patients also had an additional examination of the brain. *Results.* Our preliminary experience has shown that MR imaging permits the simultaneous evaluation of the spinal cord, vertebral column and the surrounding soft tissues. The severity of the cord and soft tissue injury was seen to be often much greater than was suggested from other more invasive radiological techniques. In several patients the information provided materially influenced a management decision in favour of early surgery. Most patients had evidence of definite spinal cord damage and, as part of an on-going follow-up study, we hope to determine which patients progress to syrinx formation or develop other complications. The operational characteristics of the equipment will be discussed and several representative examples are shown of the spectrum of MR appearances in spinal injury.

Phase III trial of oral magnetic particles (OMP) in abdominal and pelvic MRI

D. MacVicar
The Royal Marsden Hospital, Sutton, Surrey

Purpose. To evaluate clinical advantages and disadvantages of oral magnetic particles (OMP, Nycomed AS, Oslo) in an open ended Phase III trial. *Methods and materials.* OMP is a newly developed, super para-magnetic contrast agent for use in abdominal and pelvic MRI. It consists of an aggregate of small ferromagnetic crystals incorporated in polymer particle, and results in negative contrast in bowel. In a prospective study group of 35 patients, to date 15 have been examined. Patients with a variety of suspected or known abdominal and pelvic malignancies are selected from the population of an oncological hospital. Magnetic resonance imaging of the region of maximal interest is performed before and after administration of OMP using a Siemens Magnetom operating at 1.5 T with standard spin echo sequences (TR 0.5–2.1; TE 17–90). *Results.* Image quality is assessed in terms of: (a) diagnostic value; (b) distribution of contrast; (c) artefacts. Initial experience with OMP is encouraging. In the authors view, diagnostic value has been enhanced by administration of OMP in 11 out of 15 patients. Practical aspects and patient tolerance are discussed. *Conclusion.* MRI of the abdomen and pelvis still has technical and practical problems to overcome. OMP is likely in the future to find a place as an oral contrast agent in MRI.

Monitoring treatment response in bone marrow disorders using quantitative magnetic resonance and image analysis techniques

N. Roberts, S. R. Smith, D. Percy and R. H. T. Edwards
Magnetic Resonance Research Centre and Department of Statistics and Computational Mathematics, University of Liverpool, P.O. Box 147, Liverpool L69 3BX

Elevated proton relaxation times have been reported in various bone marrow disorders. To investigate whether this observation can lead to a method for monitoring progress and treatment response in Hodgkin's disease (HD), pixel by pixel T_1 relaxation time maps were computed, using software developed in house on a SUN 3/60 workstation, from six spin echo images of the lumbar spine (TR ranging from 2400 to 250 ms). Magnetic resonance data were acquired from a single sagittal midline slice of the lumbar vertebrae using a 1.5 T General Electric SIGNA system. Eighteen normal volunteers and 20 patients with HD have been studied. The outlines of the lumbar vertebra in the proton density image were automatically identified using line detection algorithms available on a Contextvision Image Analysis system. This enabled the T_1 data relevant to the vertebral bodies to be isolated. The lumbar vertebra T_1 data were found to exhibit a log normal distribution which could be characterized by the median, 5% and 95% centile values of the T_1 histogram. From the normal control T_1 data a three-dimensional 95% probability region was calculated with respect to which the patient data could be classified. Serial studies have allowed response to treatment, and the presence of residual disease to be assessed. In addition marrow engraftment following autologous marrow transplantation could be addressed by correlating alterations in T_1 on a pixel by pixel basis with haematological markers of engraftment.

T_1 and T_2 changes in patients infected with HIV

D. Kean, J. J. K. Best, A. Blane, *A. Chiswick, *R. Brettle and †G. Goodwin
*Departments of Medical Radiology and *Infectious Diseases and †Psychiatry, University of Edinburgh, Edinburgh*

It has been demonstrated that magnetic resonance imaging can detect white matter abnormalities, by virtue of increase in T_1 and T_2 values, in patients suffering from multiple sclerosis before focal lesions, *i.e.* plaques are apparent. *Methods.* In an effort to detect similar pre-clinical changes in subjects infected with HIV, MR imaging was performed on 64 HIV positive subjects. This cohort was composed of 10 homosexual males and the other 54 individuals had been infected by blood transmission (32 males and 22 females, mean age 34 years). Thirty of these subjects were re-examined a year after their initial scan and the MR measurements of both examinations compared. An SR/IR interleaved sequence (TR, 1 s; T_1, 200 ms) and a CPMG (TR, 1.5 s; TE, 32–128 ms) sequence were used to image the entire brain and from these images T_1 and T_2 measurements were obtained. The imaging device was a 0.08 T resistive system. T_1 and T_2 measurements were obtained from the corona radiata of each hemisphere and separate measurements of the frontal and parietal white matter were also obtained. Measurements were also obtained from deep grey matter structures with particular reference to the caudate. Of the patients who were re-examined, 19 remained in the same clinical stage, nine deteriorated by one stage and two deteriorated by two stages. *Results.* There was noted to be no change in either T_1 or T_2 values obtained from the hemispheres or when frontal and parietal areas were measured separately. Measurements from deep grey matter, in particular the caudate, showed slightly more variation and some of these changes approached significant levels. However, much of this apparent change could be explained by the smaller area of these structures and their closer proximity to CSF regions thereby increasing errors due to partial volume and registration errors. In conclusion, it has been shown that there are only very small, barely significant changes in cerebral T_1 and T_2 values in HIV subjects on sequential MR imaging. It would appear therefore that this form of study will require long term follow-up in a large cohort of subjects and that further refined measurements or more specific cerebral regions may reveal early changes.

^{1}H spectroscopy of normal and transplanted kidneys

N. J. Shah, T. A. Carpenter, L. D. Hall, A. K. Dixon, C. E. L. Freer, I. D. Wilkinson, C. Sims and D. B. Evans
Cambridge

It is known from ^{31}P NMR studies of other transplanted organs that the metabolic markers may provide a non-invasive means of monitoring rejection. Given the higher sensitivity of ^{1}H spectroscopy compared with ^{31}P and the greater number of potentially accessible metabolites, we have chosen to develop and implement a protocol for *in vivo* localized ^{1}H spectroscopy of the human kidney. Water-suppressed spectra were obtained by means of the STEAM sequence from a localized 3 cm cube of the kidney using a number of surface coils on a Picker International (HP2055) whole-body scanner. The number of signal averages was either 265 or 512 with a TE of 270 ms and a TR of about 2 s. We present results obtained from three patients with transplanted kidneys (1 month to 18 months post-operative) and from four normal volunteers. We believe that these results constitute a significant advance in the understanding of ^{1}H *in vivo* NMR of the human kidney. In particular, we show that a number of errors in the identification and quantification of peaks in the spectrum have been reported.

^{19}F MRS studies of brain halothane in humans

D. K. Menon, G. G. Lockwood, C. Peden, I. J. Cox, J. Bell, D. J. Bryant, J. Sargentoni and J. G. Whitwam
NMR Unit and Department of Anaesthetics, Hammersmith Hospital, Du Cane Road, London W12 OHS and Hirst Research Centre, East Lane, Wembley, Middlesex

Objectives. ^{19}F MRS has been used to study flourinated volatile anaesthetics in animals. This study reports on ^{19}F MRS studies of the brain in five patients recovering from halothane anaesthesia. *Methods.* ^{19}F MRS was performed on a 1.6 Tesla Picker prototype system (operating at 64 MHz for ^{19}F). All five patients were fit females (aged 32–45 years, ASA I) undergoing minor gynaecological procedures. At the end of the anaesthetic (0–4% halothane in oxygen) the patients were transported to the MRS suite on a purpose built trolley and spectroscopy was performed. All patients gave informed consent, and were fully monitored during transport and spectroscopy. Initial fluorine spectra were obtained between 35–80 minutes after completion of the anaesthetic. *Results.* Whole volume spectra in all patients showed a peak at 37.5 ppm (referenced to sodium fluoride at 0 ppm). Its linewidth suggested T_2^* of about 4 ms and comparison of signal intensities at repetition times of 0.5 and 5 s suggested a T_1 of 0.5–1 s. In one patient a second peak was seen at 41 ppm. This peak appeared to have a longer T_2^* (about 30 ms) and a slightly longer T_1 than the peak at 37.5 ppm. Spatial localization using one dimensional phase encoding suggested that the first peak arose form the brain and the second from the scalp.

^{1}H NMR spectroscopy of tumour and normal tissue extracts. Tissue charaterization by pattern recognition

R. J. Maxwell, S. L. Howells and J. R. Griffiths
CRC Biomedical Magnetic Resonance Research Group, St George's Hospital Medical School, London

Objectives. The information content of ^{1}H NMR spectra of biological tissues is immense. The problem of poor Bo homogeneity limits the resolution that can be achieved *in vivo* but this is partially overcome by studying tissue extracts. In order to interpret the available information it is desirable to reduce the complexity of the data. We have used pattern recognition methods to analyse ^{1}H NMR data from chemical extracts of rat tissues and tumours. The aim was to distinguish between normal tissues and tumours of various origins. *Methods.* Rat tissues and tumours were excised and frozen in liquid nitrogen. Chemical extracts were prepared using 6% perchloric acid. ^{1}H spectra were obtained at 400MHz. Data processing gave a constant water linewidth and generated normalized peak heights at 0.5 ppm intervals. Principal component analysis and cluster analysis were used to characterize the different sample types. The current database includes 58 samples (from five tumour types and three normal tissues) and has 90 variables for each sample. *Results.* The first 12 principal components accounted for most (93%) of the variance of the data. These components were used in the cluster analysis which successfully distinguished tumours from normal tissues. In almost all cases the cluster analysis could separate the different tumour types and tissue types from each other. It was notable that the well differentiated hepatoma type was closely associated with the liver cluster but the poorly differentiated hepatoma type was not.

Combined MRI an localized ^{1}H NMR spectroscopy of the brain in children

Stephen Austin, Alan Connelly and David Gadian
NMR Unit, The Hospital for Sick Children, Great Ormond Street, London

Localized *in vivo* ^{1}H spectroscopy of the brain has been performed in over 60 children referred for routine imaging studies in order to evaluate spectral changes with age and in disease. After MRI using a dual-echo STIR sequence (providing improved contrast in the assessment of myelination), 8 ml cuboidal volumes of interest were selected on the basis of imaging and clinical information. Localized spectra were then obtained using a spin echo technique. Watersuppression was achieved by a single Gaussian presaturation pulse. Signals are routinely observed from N-acetyl aspartate (NAA), total creatine (CR) and choline-containing compounds (Cho). NAA/Cr and NAA/Cho signal ratios increase wiht age, whereas Cho/Cr falls. Regional variations are also observed. NAA is believed to be located primarily within neurons, and reduced NAA ratios have been observed from various focal lesions and from abnormal white matter in certian leukodystrophies. This suggests a role for the NAA signal as a marker of neuronal loss. In Canavan's Disease (in which NAA breakdown is impaired), NAA ratios are extremely high, and this appears to be a specific finding. Lactate has been demonstrated in certain disorders, including pyruvate dehydrogenase defeciency, and can show regional variations.

1991, The British Journal of Radiology, 64, 81–84

Book reviews

MRI of the Body. Ed. by D. Vanel and M. T. McNamara, pp. xxiii + 385, 1989 (Springer-Verlag, Berlin), DM 398.
ISBN 2-287-00013-5

The aim of the book is to describe the basic principles of magnetic resonance imaging (MRI) and to survey its current status in clinical applications throughout the body. In common with many MRI texts, the early chapters on the physical basis of MR are adequate, the glossary is fairly comprehensive and the chapter on artefacts useful.

The subsequent 24 clinical chapters contributed by some 50 French and Belgian radiologists are of varying quality. However, in the main, each chapter is too brief to do justice to it's subject. The description of examination techniques and choice of sequences for each section is too repetitive, especially as nearly all the illustrations in the book are of either short or long echo sequences; gradient echo and inversion-recovery images are under-represented.

The failure of the attempt to be comprehensive is best exemplified in the chapter on joints. This gives a very fleeting impression of the current status of MRI in this area. The oncology chapters are better, particularly those on paediatric oncology and bone marrow disease.

Though valuable information is given in many chapters, the content is on the whole too sketchy to provide a reliable reference text. Recent improvements in imaging sequences and surface coils have also made most advice on imaging techniques out of date. Although the illustrations are of good quality and the chapters are well referenced up to 1987, it is hard to justify the cost of DM 398.

H. Baddeley

Adrenal Disorders. By E. Darracott Vaughan Jr and R. M. Carey, pp. xi + 304, 1989 (Georg Thieme Verlag, Berlin), DM 144.
ISBN 3-13-664801-3

The editors of this book state that it has been written primarily for the physician who deals with adrenal disease in clinical practice. The have aimed to provide an up-to-date review of adrenal disorders with an emphasis on clinical management, from appropriate biochemical investigation to medical and surgical treatment.

The volume starts with the basics — adrenal anatomy, histology, embryology and pathology. There follow chapters on general biochemical and radiological investigation before the main body of the book, where each type of adrenal disorder is given a separate chapter, with detailed discussion on the possible treatment options as well as suggested investigation strategies. Strangely, the final chapter reverts to investigation, covering magnetic resonance imaging (MRI) of the adrenal. The fact that six out of the 22 American contributors are radiologists presumably reflects the important role radiology plays in the investigation of patients with adrenal disorders. It is disappointing to find therefore that, apart from the radiological section ("Sectional imaging of the adrenal glands: computed tomography and ultrasound") and the MRI section, there appears to be no radiological input into the remainder of the book. This would be of less importance if there was an adequate section on the complex subject of radio isotopic techniques, but unfortunately there is only a brief mention of iodocholesterol and MIBG scanning at the end of the radiology chapter. The coverage of nuclear medicine outside this chapter is variable and in some places simply incorrect. For example, in the section on Conn's syndrome, the use of radio-iodinated cholesterol is dismissed as being unreliable, and no mention is made of the importance of steroid suppression of the adrenals. In the discussion of the management of incidentally discovered adrenal masses, no mention is made of the useful role iodocholesterol scanning can play in deciding which patients require further, more invasive investigation. No mention is made of MIBG in the chapter on phaeochromocytoma, and the reader is referred (erroneously) back to the chapter on Cushing's disease. In the brief mention of MIBG in the radiology chapter, it is not stated that ^{131}iodine is an unreliable tracer and that ^{123}iodine is the agent of choice. One is left with the feeling that each of the contributors was under the impression that someone else would be writing a definitive section on nuclear medicine! Despite these criticisms the book is well written, although inevitably, as occurs in most multi-author textbooks, there is some repetition. It is comprehensively referenced — there are 322 references after one 50-page chapter. The photographs are of high quality, and there are excellent line drawings of the various surgical techniques.

This book might be of use in a medical library, where I suspect that it would be of some value to both physicians and surgeons. However, the clinical and biochemical content is too great and the radiological content too small for it to be recommended to general radiologists.

Mary E. Roddie

Tuberculosis of the Skeleton. By C. J. Thijn and J. Steensma, pp. x + 171, 1990 (Springer Verlag, Berlin), DM 298.
ISBN 3-540-51017-6

This small book serves to remind us that tuberculosis has not been eradicated in the Third World, and indeed is increasing even in nations with better than average health care, particularly as a consequence of AIDS. The material illustrated is based on a study of 370 patients seen in The Netherlands over the period 1955–1987.

The text is brief but adequate, and in many respects this could be regarded as an atlas. The early text covers pathogenesis, clinical findings, diagnostic methods and epidemiology. Atypical mycobacteria and BCG osteomyelitis are discussed. Thereafter, the book addresses the regions involved, beginning with the most common site — the spine. In each section the authors wisely begin with illustrations of the more typical radiographic appearances before showing the variations that may be encountered. A list of possible differential diagnoses is provided. The site and types of the 460 skeletal lesions are comparable to those of other large series, and this is tabulated.

The reproduction of the radiographs is excellent; linear tomography and the occasional computed tomography (CT) and magnetic resonance (MR) image are provided, more examples of such imaging in the more recent clinical material might have been valuable. The value of bone scintigraphy is not mentioned in the section on diagnostic methods, although it gets a very brief mention in the sections on the spine and arthritis.

It was a surprise to find that the authors prefer open biopsy for skeletal lesions to the less invasive and less destructive percutaneous approach, which provides an equivalent number of positive cultures and obvious benefit to the patient. I have few faults to find with this book: only the occasional word *e.g.* gonitis, spondylodesis anterior and hydrops (of the joint) reveals its European origin. The authors seem to use the term *spina ventosa* synonymously with tuberculosis of a phalynx, whereas it should be reserved for a specific appearance. I would challenge a few statements, *e.g.* if fibrous adhesions of the joint cavity are formed narrowing of the joint space results; usually pyogenic osteomyelitis does not penetrate the growth plate; vertebra plana is commonest in the lumbar spine, but these are minor personal contradictions.

Study of this book will remind the reader that the main reason why tuberculosis is not diagnosed clinically and radiologically is that its presence is not considered. It deserves a place in every departmental library and should be compulsory reading for all radiological reporting. Senior house officers in the orthopaedic and accident services would also gain great benefit. At the present exchange rate, it is expensive and few radiologists in the United Kingdom will wish to buy personal copies.

Perhaps in this way, the tragedy of a patient with an untreated, yet treatable disease may be avoided.

DENNIS STOKER

Gastrointestinal Radiology Reviews. Vol. 1. Ed. by H. Herlinger and A. Megibow, pp. x + 289, 1990 (Marcel Dekker Inc., New York), $132.00.
ISBN 0-8247-8099-X

In the preface, the editors state that they believe this entry will make a positive contribution to gastroenterologic literature, since it incorporates features not shown by others of its genre. It welcomes inclusion of material by authors who normally publish in foreign languages, and reviews the historical background and clinical relevance of the subject matter. It is intended as a yearly publication.

This review consists of 14 chapters by contributors from North America, UK, Japan, France and Belgium nearly all of whom already contribute to English language journals. The material covers techniques of transjugular liver biopsy, percutaneous gastrostomy, drainage of pancreatic pseudocysts and gallbladder intervention. Other reviews cover computed tomography (CT) in hepatic vascular disorders, CT following lipiodol in hepatocellular carcinoma and CT of acute small bowel abnormalities. Magnetic resonance (MR) of the alimentary tract and of hepatic tumours also receive attention. There is a review of small bowel lymphoma illustrated by six case studies, a specimen study of Peyer's patches and a chapter on transrectal ultrasound.

Although published in 1990, many of the reviews only include references to material published up to 1986. Several reviews, particularly of MR, are not as up to date as would be expected in such a rapidly advancing field.

The volume is well illustrated. The case studies of small bowel lymphoma are particularly well illustrated with corresponding pathological specimens. The text generally reads well, although the review of dynamic CT in hepatic vascular disorders leaves the reader bewildered. The arrangement of reviews in the volume does not follow a logical pattern, complementary papers are scattered rather than being grouped together.

This first volume is in some respects disappointing in not being as up to date as might be expected. In general, there is little in this first volume that cannot readily be found in the major English language radiology journals. If the editors can manage to get a little more up-to-date material into the next volume, it may make a positive contribution to gastroenterologic literature.

ALAN GRUNDY

Management of Oral Cancer. By N. Stafford and J. Waldron, pp.viii + 214, 1989 (Oxford Medical Publications, Oxford), £30.00.
ISBN 019-261609-9

This is a compact volume of just over 200 pages, edited by two ENT surgeons, with contributions from six other surgeons, an anatomist, a pathologist and a radiotherapist. It deals with cancer of the oral cavity and oropharynx, concentrating mainly on squamous carcinoma with only a brief mention of other types of tumour.

The introduction states that this book sets out to give a practical statement of views on management of oral cancer from one head and neck unit, but not to be an exhaustive work on the subject. It stresses joint management and condems any competitive stance between surgery and radiotherapy. It starts with a very detailed chapter on anatomy, followed by a chapter on pathology which is especially good on explaining the diagnostic pitfalls facing the pathologist. There is a section on the principles and practicalities of radiotherapy and chemotherapy which is fairly brief. More explanation of the biological principles and relative clinical merits of pre- and post-operative radiotherapy would have been helpful. Chapters dealing with general principles include surgical reconstruction which is very clearly described.

There are sections dealing with tumours arising at the various anatomical sub-sites in the oral cavity and oropharynx and management of the cervical lymph nodes. In all of these there is a brief statement of management policy, a paragraph or two about radiotherapy, and several pages on surgical technique. There is little or no discussion about the relative merits of different approaches to treatment and a very limited bibliography. For most early primary tumours surgery and radical radiotherapy are stated to be alternative treatments, but with no indication of factors which would lead the authors to choose one or the other in the individual patient. Some of the statements in the brief radiotherapy sections are surprising, *e.g.* the advocacy of combined external beam and interstitial radiation for early tonsillar carcinoma, and the assertion that iridium hairpins should not be used for implanting tumours of the tongue as they tend to work loose.

In general this book is well written and the material clearly set out without repetition. The black and white illustrations are clear. However, there is a rather irritating number of misprints and spelling mistakes, *e.g.* "iridium" is mis-spelt throughout. This book will be of use mainly to surgeons. Radiotherapists and oncologists will find it a useful source of acquaintance with the various surgical techniques in current use, but there is less to be found on the non-surgical management than in most standard text books.

J. M. HENK

Urologic Pathology with Clinical and Radiologic Correlations. Ed. by A. Someren, pp. xi + 755, 1990 (MacMillan, London), £76.00.
ISBN 0-02-413750-2

As its title suggests, this multi-author text, written by 28 pathologists, radiologists and urologists from the Emory University School of Medicine in Atlanta, Georgia, seeks a multidisciplinary approach to urological pathology.

The book is divided into seven chapters, with varying numbers of contributors to each, covering urological kidney disease, the urinary passages, renal transplantation, the prostate and seminal vesicles, the testis and paratesticular structures, the penis and scrotum, and the adrenals. Each chapter is preceded by a table of topics covered, and starts with sections on normal development and structure, radiological evaluation, specimen preparation and developmental anomalies.

The text is well laid out in double columns and the system of headings and subheadings is easy to follow, although there are a few minor irritations such as the occasional misquoted reference, typographic error (clump kidney, p. 26, aneurysuis, Fig. 1-97) and transposition of figure captions (Fig. 4-48 for 4-49).

For pathologists, the coverage of all aspects of urological pathology, including newer techniques such as fine needle aspiration cytology, is excellent and I found no important entities that were not included. Sections such as those on tumour pathology and renal transplantation are particularly good, and packed with useful practical information. In general, the text is as up to date as could be reasonably expected in a multi-author volume addressing a rapidly developing subject.

The book is lavishly illustrated with black and white pictures. The radiographs, ultrasonograms, computed tomography and magnetic resonance imaging scans are excellent, but a proportion of the photographs of gross specimens and some of the photomicrographs are dark and have lost detail in their reproduction. This is a pity since, in general, they have been well chosen to illustrate the entity under discussion.

As a pathology text, this book compares well with other recent publications in the field such as Murphy's *Urological Pathology*, although the standard of the pathological illustrations in the latter are often better. However, the strength of the present work lies in the careful correlation of the radiological and pathological aspects of urological disease. The advent of modern imaging techniques has rendered many of the more subtle aspects of gross morphology, traditionally the province of the histopathologist and morbid anatomist, to be readily apparent to the radiologist examining the intact patient. This has had an obvious impact in terms of more accurate diagnosis and a more rational approach to clinical management, but requires a pooling of knowledge and experience from radiologists, clinicians and pathologists.

This book clearly, and, in my view, very successfully follows this "team" approach to urological diseases. It is to be highly recommended to pathologists who seek and active role in the investigation and management of patients, and to radiologists who require a better understanding of the pathological entities with which they deal. Urologists will acquire from this book a comprehensive guidance as to how their colleagues, in the investigative specialties, can help them in the diagnosis and management of their patients.

The book is very reasonably priced, at a level to make it accessible for personal use by specialists in the field. It should certainly find a place in all pathological, radiological and urological departmental libraries.

R. A. RISDON

Commissioning and Routine Testing of Mammographic X-ray Systems (Report 59). By M. Fitzgerald, D. Dance, K. Fisher, C. Lawinski and M. Ramsdale, pp. viii + 60, 1989 (Institute of Physical Sciences in Medicine), £9.80.
ISBN 0-904181-58-8

This is a comprehensive booklet of mammographic equipment tests. Its main commendation lies in practical advice which accompanies the tests; as such it is excellent. The attempt to wrap the tests up in the language of quality systems is not entirely convincing (Ch. 2). "Commissioning" and routine tests are said to comprise the operating techniques of quality control. They are essentially inspection methods. Such methods need to be part of a quality system if they are to have purpose, but from the text it is not entirely clear how, and, the extent to which the outcome influences the quality of breast screening.

It might be held that these routine tests are inspection methods to verify the competence of installation and maintenance. If this is the case, then they should be specified as such, as an essential component maintenance contract.

A quality component specified in the maintenance contract represents a more satisfactory approach, since the feedback is systematically incorporated in a performance control schedule. A maintenance contract represents money paid to restore the equipment to its purchase specification (BS 4728). The ultimate value of an isolated routine checking regime is questionable in the context of total quality management of good imaging.

A preferable categorization of these tests might have been (a) user checks; (b) checks to be included as part of the monitoring; and (c) exceptional periodic performance trend maintenance. These comments are philosophical but, nontheless, essential if quality assurance is really to be effective. However, they should not be taken to detract from the essential core of the book which is helpful and sound both scientifically and technically.

J. A. GARRETT

Clinical Neutron Dosimetry. Part 1: Determination of Absorbed Dose in a Patient Treated by External Beams of Fast Neutrons. (ICRU Report 45), pp. x + 90, 1990 (ICRU Washington, DC).
ISBN 0-913394-39-4

This ICRU report maintains the standards of previous ones and will be an essential guide for every department concerned with neutron therapy. It is intended to do for neutrons what *Report 29* did for photons and electrons. It is also a successor to *Report 26* but does not supersede it as little in *Report 26* is repeated.

The contents of this report cover a wider field than the title suggests. In addition to dosimetry the report discusses neutron spectra and their methods of measurement, microdosimetric characteristics, neutron production and beam characteristics. Biological factors are reserved for a later report. Radiation protection against neutrons is also excluded. There are no tables of data corresponding to those in *Report 26*.

This report discusses, in detail, the current internationally agreed protocol for determining the absorbed dose at the reference point in a water phantom, using tissue-equivalent chambers calibrated in a standard beam of photons. The gain in precision by using a calorimeter is pointed out. Other points discussed include discrimination between neutrons and gamma rays, *in vivo* dosimetry and dosimetry intercomparisons. The final chapter is concerned with distributions of absorbed dose in patients, including kerma ratios, corrections for inhomogeneities, interface effects and treatment planning.

As usual with ICRU reports, the standard of presentation is excellent. My only cavils are that there are virtually no references after 1985 and that equation 2.6 lacks a minus sign in the exponent.

D. K. BEWLEY

Clinical NMR Spectroscopy (Report 60). Ed. by J. Dykes and D. Delpy, pp. 91, 1989 (Institute of Physical Sciences in Medicine), £14.00.
ISBN 0-904181-57-X

This concise book summarizes an extensive range of presentations on developments in magnetic resonance spectroscopy and relevant magnetic resonance imaging as of 1987. At the time of review (1990) it is evident that there has been an unfortunately long delay between the verbal presentations and the appearance of the public proceedings. This clearly limits the value of the book as an up-to-date account of recent developments in the field. It does, however, represent a valuable compendium of physical principles underlying the clinical applications of MR spectroscopy.

The text opens with useful considerations of what are the desirable measurements and the physical limitations of spectroscopy, together with the considerations underlying the need for spatial resolution in *in vivo* MR spectroscopy. The second section summarizes clinical experience in the application of spectroscopy to the study of the composition of the brain in newborn infants, the follow-up therapy in human tumours and the extension of applications to nuclei including 31P, 13C and protons. The underlying considerations are those of the importance in signal to noise ratio and the benefits and costs of various MR techniques for spatially resolved spectroscopy. The final section deals with associated techniques including the use of labels and contrast agents in MR spectroscopy and imaging. These agents include deuteurium and the use of 13C enriched substrates such as [3-13C] L-alanine and [1-13C] glucose. In imaging much has already been learnt of the use of paramagnetic labels such as gadolinium compounds Gd(III)DTPA. The volume finishes with an interesting section on methods of evaluating susceptibility effects and their potential impact on *in vivo* spectroscopic studies.

As with other proceedings of scientific meetings this volume contains an abbreviated discussion at the end of each of the chapters. This provides further insights into the degrees of uncertainty of different methods and to possible solutions to technical problems. The authors of the individual chapters are leading scientists in the field, working in European centres. The subject area is thus well covered, briefly but with authority, and should be of interest to hospital physicists and clinicians interested in MR imaging and spectroscopy.

The book reads well and has a large number of well prepared illustrations. It is economically priced. As a short book in a rapidly expanding market in which most of the texts are very extensive, this book certainly has a place. Yet it is regrettable that it has taken so long to reach the point of review.

R. H. T. Edwards

Radiation Therapy of Benign Diseases. By S. E. Order and S. S. Donaldson, pp. viii + 212, 1990 (Springer-Verlag, Berlin), DM148.
ISBN 3-540-50901-1

The duty of a doctor is to his patients. This duty aims to preserve the patients' peace of mind either by curing the disease complained of or by ameliorating the symptoms and, in all cases, by preserving or restoring self confidence and maintaining confidence in his doctor. In malignant disease this is difficult for the patient who thinks his condition is likely to be fatal. For treatment of benign conditions, the association of radiation exposure with leukaemia and other types of cancer causes difficulties for the patient and for the radiotherapist, over whom hovers the shadow of litigation if anything untoward should appear to result from treatment.

This book wisely introduces the necessity for informed consent, as part of the standard of care, required of the radiotherapist through the eyes of a widely experienced legal expert. The patient should understand his condition, the treatment, and what to expect if not treated as contrasted with the effects of treatment. The "radiation oncologist who faces an occasional rare, non malignant disorder" is for many benign conditions, not acting as an oncologist but as a radiotherapist. For many benign tumours the likelihood of repeated recurrences terminating in widespread metastasis, emphasizes the need for first time elimination of the tumour, using brachytherapy in conjuction with conservative surgery. This would be more effective than external radiation (Table, p.201).

Insight into other conditions such as fungal infections, pyogenic and viral infections, auto-immune conditions and diseases of unknown etiology would require greater knowledge and experience than is possible for most doctors and certainly for most oncologists. The referral to a radiotherapist of an occasional rare case, which has proved either too difficult or is recognized as requiring radiation, is a custom that is likely neither to build up nor to call upon the necessary expertise of many radiotherapists. This book quotes much historical data and provides many published results, which are of variable value to the radiotherapist. Some of this data came from the 1940s when clinical impressions and follow-ups, in spite of poor dosage calibration and lack of randomized comparisons, gave some useful results. Most of the information given ranges from 1960 to 1988. The advice by the authors under the individual disease headings is very valuable when it is given.

Featured in the book are the results of a National Survey of Radiotherapists' opinions which, indicate to me, by refusal to treat many conditions, a degree of caution due to lack of experience and anxiety to avoid adverse litigation. This might well be reversed by the use of this book as a general superficial survey of radiation therapy for benign disease and as a reference book to be used when a patient is referred with one of the 78 diseases that are alphabetically listed. The relevant publications can be consulted quickly to supplement the guide lines given by the authors. This will enable the radiotherapist to give as good an opinion and decision as he can; if he has first hand experience and knowledge of such a case, so much the better.

A section on the principles which could be used as a guide for treating the varied conditions by radiation would perhaps improve the value of the book. Included could be a paragraph on the imperative need for complete energy, dose, time and fractionation details of any course of treatment. Before 1939 when sulphonamide antibiotics were not available there were many more treatments of benign disease by radiation. For example, local radiation was used in the treatment of gas gangrene and has saved many limbs from amputation. A book on this specific topic was written by Murphy in the 1930s.

F. Ellis

Sectional Anatomy by MRI/CT. By G. Y. El-Khoury, R. A. Bergaman and W. J. Montgomery, pp. xiii + 733, 1990 (Churchill Livingstone, Edinburgh), £125.00.
ISBN 0-443-08543-9

This atlas contains a comprehensive set of magnetic resonance images of the limbs, thorax, abdomen and pelvis in coronal, sagittal and axial planes. In addition, contrast enhanced computed tomography (CT) is used to demonstrate the heart and great vessels as well as the abdomen. Each image is annotated by salient anatomical points, usually related to muscle attachments and the course of vessels. Anatomical features on the images are labelled in a full, clear and unobtrusive style. The illustrations are of a high standard. Regions of interest are easily located and there is a very extensive index.

This atlas is recommended as a bench book in magnetic resonance imaging (MRI) units and as a revisional aid for trainees. However, the exclusion of the head and neck may limit its function in this regard.

G. H. Whitehouse

1991 The British Journal of Radiology, 64, 85–86

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Honorary Editor, BIR Bulletin: D. Rickards, LRCP, MRCS, FFR(D)SA, FRCR
Please address all correspondence to: Honorary Editor, BIR Bulletin, The British Institute of Radiology,
36 Portland Place, London W1N 4AT
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How Can UK Professionals Help to Support Imaging Services in Developing Countries?

Report of a Workshop Meeting, 5 July 1990

Prepared by M. Gowland, C. R. Hill, A. B. Strong and N. G. Trott

The meeting had been arranged in workshop format, with the intention that all participants would contribute. The object of the workshop was to reach a consensus on how professionals in the UK are best able to help to support medical imaging services in developing countries, and in particular to consider which areas of expertise will be most useful, what will be the most effective form of support, whether support should be concentrated on a single site or be more widely distributed, what sources of funding might be available and how our support should be co-ordinated with other bodies. The meeting had the support of a number of such bodies and, in particular, Dr Hanson from the World Health Organization (WHO) and Dr Buchanan from the British Council were both contributing to it. Many letters of support had also been received, including one from Lady Middlemiss and one from Professor Palmer, a principal WHO consultant, who were, unfortunately, unable to attend.

Of the three sessions into which the meeting was divided, the first two, under the chairmanship respectively of Professor Rhys Davies and Mr Mick Jordan, were devoted to brief presentations and discussion on particular topics. The third, a "workshop" session, jointly chaired by Dr Hanson and Professor Hill, then sought answers to specific problems and a plan for further action.

Part 1

Topic Presentations

A. Activity of existing organizations — are there gaps?

The WHO activities in medical imaging in developing countries

Dr G. Hanson
Chief, Radiation Medicine, WHO, Geneva

Dr Hanson first outlined the structure of the WHO, then the problems facing developing countries and finally how WHO functions in relation to these problems, which are demographic, economical and financial. The world population of 5 billion at current rate of increase will reach 11 billion by the end of the 21st century and is then expected to plateau. The proportion of elderly in the population is increasing: 1 in 15 of the population will be over 65 in the year 2000. As the age of the population increases, the causes of death in rich and poor countries become more similar, so that in developing countries death from malignant disease and cardiovascular causes increase in importance and deaths from infectious disease diminish.

Since 1980 there has been a downturn in the economic situation for all developing countries, with the possible exception of South East Asia where there has been some growth. The current gross national product per capita in the developing world is around $500 (having *reduced* in Africa and East Asia, for example, by between 20 and 40% since 1980) and in most countries less than 5% of this is spent on health. Cuts in education as well as health spending have taken place, which have been illustrated by the declining literacy rate. Cuts in military spending are not so marked. It would be natural to assume that, as the economic plight of developing countries worsened, there would be an increase in support from the richer countries. But this is not the case — in fact there has been a reversal in the flow of cash between the rich and the poor. In 1979 $40 billion moved from the rich northern hemisphere to the poorer south, whereas in 1988 $20 billion moved in the opposite direction from poor to rich! The reasons for this startling reversal are the rising cost of debt repayments coupled with falling commodity prices.

The disease patterns in the Industrialized and Developing Worlds are very different. The percentage of cases of the total are for example:

Disease	Industrial	Developing
Neoplasms	19%	5%
Circulatory	54%	19%
Infectious	6%	40%

Thus any consideration regarding imaging must take these patterns into account. Despite the magnitude of these demographic and economic problems, by far the greatest problem facing developing countries is financial.

Eighty per cent of imaging services are in the major centres and so for large numbers of the population they are too far away to be used. Of the imaging equipment which is available, between 30% and 60% will be out of order at any one time, which inevitably causes and increases waiting time for an already overloaded system, thus severely restricting this service. There is a variable quality in clinical usage and so the limited service provided may not always be related to clinical need, further reducing its clinical effectiveness.

To assist with these problems the WHO has a Radiation Medicine Programme which embraces radiography, nuclear medicine and ultrasound. Its activities include preparation of manuals for the use of those operating the imaging equipment, for doctors not trained in the interpretation of images and for those involved in maintenance of equipment. The aim in the future is away from importing imaging equipment into developing countries and towards the manufacture of equipment in the countries where it is needed. The WHO is also working towards a rational approach to radiodiagnostic investigations on the grounds that the medical use of radiation is the major source of exposure of the world population to ionizing radiation and that overused and misused diagnostic radiographs represent completely unecessary radiation exposure (WHO, 1983, 1987). To support this approach further it has produced a quality assurance booklet in diagnostic radiology with English, French and Spanish translations (WHO, 1982). The WHO does not work in isolation but in close collaboration with other organizations: international organizations, governmental agencies, collaborating societies, WHO advisory panels and non-governmental organizations such as the BIR.

The mechanism of referral from the initial point of contact between patient and medical help is important. Where appropriate, the patient will be referred to a more specialized unit, where expert help will be concentrated.

The WHO is organizing a meeting in November 1990 on the functions at the first referral level to address this subject.

The training of radiologists

Dr J. E. Williams
Warden, The Royal College of Radiologists

In medicine today imaging is essential to clinical care. The role of the Royal College of Radiologists is to set standards of imaging practice and to ensure that these standards are maintained. Imaging should be introduced as a basic part of clinical practice in the instruction of medical students so that from the outset they are aware of its importance.

For those wishing to train as radiologists in the UK or overseas there are two qualifications: FRCR and DMRD. FRCR may be taken after a 3-year period of training and is recognized as a high standard of radiological training. FRCR is the qualification essential to obtaining a Consultant post in the UK and is obligatory for obtaining accreditation with the Royal College of Radiologists. DMRD involves either 2 years training in a recognized UK Department or 2 years training overseas in unrecognized departments plus 1 year in a recognized UK department. DMRD is not recognized for a Consultant post in the UK.

There are several options open to doctors from abroad who wish to train as radiologists.

1. Train in their own country and obtain their national qualification.
2. Train in training departments recognized by the Royal College of Radiologists in their own country and obtain the FRCR and/or DMRD.
3. Spend up to 4 years training in UK and obtain the FRCR and/or DMRD.
4. Train part-time in UK *e.g.* 1 year sabbatical, 1–12 months spent acquiring extra expertise in a particular area, Overseas Doctors'

Training Scheme, exchanges with trainees from UK etc. but not in preparation for FRCR or DMRD.

5. Train under visiting teachers to their own country. This may be a more cost effective method of training. Small teams of experts visit developing countries for short periods to give instruction and training. More trainees in radiology can benefit form this teaching than would be able to travel to UK to be taught. Individual professors or fellows may spend longer periods abroad giving practical hands-on instruction as well as the more formal lectures and seminars.

The Radiology Outreach Foundation — its aims and achievements

Professor I. Isherwood

This is a new organization, established in 1988 to provide equipment, books and training in radiology to healthcare practitioners in medically disadvantaged countries. It is a non-profit-making organization, controlled by a board of directors all of whom come from internationally recognized academic radiology departments. There is also an international Advisory Board with representation form industry and radiology from 20 different nations. The Foundation organizes donations of books, journals, equipment and expendables, *i.e.* chemicals, films, etc. It is important to recognize the need for infrastructure support, hence the inclusion of representatives from industry on the Advisory Board. It is not just the Third World who should be considered medically disadvantaged but also, in the immediate future, Eastern Europe should be included. The Foundation endeavours to send teachers to countries in need, not just one-off personal visits but possibly also video cassette teaching tapes which could be updated, *e.g.* on a monthly basis, thus extending the period of usefulness of the teaching. Teaching materials can also be made available and help given with the organization of teaching programmes. The aim is to foster professional liaison with the medically disadvantaged countries, to encourage support for radiology and to assist in the provision of training in these countries.

The role of the International Society of Radiographers and Radiologic Technicians (ISRRT)

Mr M. Jordan

The College of Radiographers

Mr Jordan spoke as an official of the ISRRT, an organization which embraced 59 national societies and 57 different countries and whose objective is to assist developing countries attain their medical imaging requirements. The emphasis is on listening to the needs of each country as perceived by that country and meeting those needs rather than dictation what the needs should be. The ultimate aim is to extend medical care and, therefore, medical imaging to all those who are in need of it. The ISRRT is active in the promotion of improved standards of training and research in the technical aspects of radiation medicine, and believes that radiographers should be involved in the decision making and training that this entails.

Discussion

The first, very practical, point raised in the discussion was sending personal copies of radiology journals to developing countries. Is it permissible to do this and if so how can it be done most effectively? It was not possible to give the official policy of the BJR on this question but Professor Hill (President of the BIR) believed that the BIR would support individuals disposing of their journals in this way. There was no known co-ordinated system through which such journals could be sent but is was suggested that organizations such as VSO may be able to help. However, if it is done it is essential that full postage is paid.

A question about the overseas doctors training scheme (ODTS) was then raised. In theory this was excellent but in practice there were insufficient posts available, as all were occupied by career radiologists. The difficulty is that radiology is a shortage specialty and there is an emphasis on increasing the number of UK consultants. However Dr Williams indicated that the RCR intends to operate a form of clearing house system whereby posts which become available for ODTS, together with sponsors for these posts, can be paired up with suitable applicants.

The final point raised in discussion was about the duplication of effort. In this context it was suggested that the World Radiographers Trust Fund mirrored the Radiology Outreach Foundation and it was agreed that the two bodies should co-ordinate to avoid any wasteful duplication.

B. Learning the hard way — lessons of experience

UK prison services' radiography

Dr K. Tonge

Working in Brixton, Dr Tonge is part of the Home Office Directorate looking into the provision of X-ray services. The need for an imaging service is substantial; for example, because of the high incidence of TB together with the inevitable overcrowding in prisons, each inmate needs at least one chest radiograph during his stay in prison. The cost of obtaining this service outside the prison, because of the cost of escorts etc., is exorbitant, and so there has to be provision in house. This provision is usually very basic: a single room shared with paramedical services such as physiotherapy, ophthalmology etc., often old equipment, maybe a portable X-ray machine. In addition to these deficiencies, the directorate also found that there was insufficient technical supervision, sometimes just one weekly visit to the unit by a single radiographer. Dr Tonge compared the situation in the prison service to that in developing countries with a low budget and lack of trained personnel and suggested that these similar problems might respond to similar solutions.

Radiodiagnosis and the health service in developing countries

Dr S. K. Morcos

In developing countries, where the demand for health care and, therefore, imaging services is high, not only is there a deficiency in equipment and trained personnel, but the resources which are available are situated for the most part in the major centres and may be totally lacking in rural areas. The difficulties are further compounded by the fact that a large part of what is available is concentrated in the private sector. A potential solution to this problem of uneven distribution is a progressive referral system (as mentioned previously by Dr Hanson): patients are seen first in peripheral medical units; if there is a need they are then referred on to a first level hospital equipped with basic imaging facilities and if necessary on from there to a tertiary referral centre where there are more sophisticated facilities. The WHO Basic Radiological System (BRS) has been recommended as the equipment of choice for the first level hospitals but at a cost of £40 000 it is probably too expensive. Ultrasound is a cheaper imaging modality in terms of equipment but is more operator dependent and so the cost and/or availability or personnel to use the equipment becomes the limiting factor. Training personnel and maintaining the standards of those already trained is a major problem. The various possibilities for this have already been outlined by Dr Williams. Liaison with radiological societies and medical schools, possibly with some form of access to X-ray museums and libraries, together with regular teaching visits from these institutions, are potential methods of maintaining standards of those providing imaging services in developing countries.

Strengths and weaknesses of a Third World X-ray department

Dr G. Harverson

Dr Harverson has had first hand experience of providing a radiology service in the Third World. As a "Middlemiss Fellow" he spent some time in Uganda and, after completing his training, went to work in a rural mission hospital in Thailand. He outlined many of the practical difficulties he had encountered: the pathology he saw was often gross and the disease pattern so different from that in the West that tropical radiology was almost a distinct specialty; conditions were so basic that fogged film was a regular problem; clinical users, not well versed in modern radiological techniques, did not always make best use of the service available and communication with these users was difficult. There were also some positive aspects. The hospitals, being small, were not bogged down by bureaucracy and so it was possible to implement change and see improvements as a direct result of them.

Discussion

There was some debate about BRS. Was it acceptable for experts in the West to recommend the use of this equipment in developing countries when it was not in use here? If, however, it was the most appropriate equipment in the Third World and cost its only limitation then perhaps our role should be to put pressure on manufacturers to lower the cost, perhaps through manufacture in a low-cost economy.

Regarding the problem of adequate training in radiological imaging, it was noted that the Wellcome Trust are using compact disc systems to make interactive training programmes. Provided the hardware could be made available and maintained, this might well be a more economical means of training than current methods which involve expensive travelling by either the trainers or the trainees.

C. The need for training — who, how and where?

Radiology training in Malaysia

Dr M. L. Wastie

Malaysia has a population of 16 million, consisting of approximately 55% Malays, 35% Chinese and 10% Indians. There has been much progress in the provision of medical care in Malaysia in recent years with the building of several large modern hospitals with up to date imaging facilities throughout the country. There are, however, still problems, *e.g.* shortage of trained personnel and unequal distribution of their expertise. It is not possible for doctors working in the public sector to undertake private practice and, although there are six times as many public sector beds than private beds, fewer than half the doctors work in the public sector. In 1983 the degree of Master of Medicine in Radiology was started and to date 11 radiologists have qualified from it but there is still an acute shortage. According to figures produced by the Malaysian Medical Association, at the present rate of growth there will be in 1995 a deficit of 132 radiologists from the 215 needed to provide one radiologist per 150 000 population.

Radiological education in Kenya

Dr J. F. Calder

Dr Calder was DMO in Malawi for 2 years and 6 months prior to training in radiology and saw then not only the deficiencies in radiological facilities but also the inappropriate way in which available facilities were being used owing to lack of training. In 1962, when training in radiology began in Kenya, there were two radiologists, one in the private sector, one in the public. Between 1966 and 1980, when there was a training link between Kenya and the Department of Radiology in Bristol, 12 radiologists were trained but there was a significant amount of wastage: only five of those trained ultimately practised in the public sector in Kenya. In 1977 a masters medicine course began and the first four radiologists graduated from this in 1980 but, for political reasons, the University was closed in 1982 and so this is no longer available. By 1983 there were still only 22 radiologists, seven in private practice and 15 in government service, the majority of these based in the large centres, Mombassa and Nairobi. The shortage is becoming progressively worse as the population of 20 million is growing much faster than the number of radiologists. Of course shortage of trained personnel is not the only problem and there would be little value in training more people if the equipment for them to use was not available. And again there is no guarantee that radiologists, once trained, will stay and work in Kenya. The small mission hospitals often provide a more effective service than the larger government hospitals and one possible solution might be to train local people to provide a very basic service in these hospitals.

Ultrasound training programmes for medical and paramedical personnel

Mrs J. Fisher

Mrs Fisher is tutor at the Manchester School of Radiography based at Salford College of Technology. The college is active in forming links with colleges overseas and has several training schemes in operation or under development. Currently a student from Nigeria, sponsored by the British Council, is studying on the Diploma in Medical Ultrasound course, some learning packages have been written in Salford and these packages are delivered by local qualified trainers. In conjunction with equipment manufacturers the school is considering preparation of courses in basic ultrasound training to be held in Manchester, specifically for medical and paramedical personnel from developing countries, and these basic courses will be followed by advanced skill courses. The low cost of ultrasound equipment may make it more readily available than the more costly imaging modalities and therefore ultrasound training is a very appropriate area to begin such training schemes.

Discussion

The possibility of a situation arising in the future when there were sufficient trained radiologists in the Third World to provide training locally and so obviate the need for training from abroad was discussed. It was felt that, although progress was being made along these lines, for example in Nairobi, there would always be a need for some contact with the West.

There were several references to wastage of trained people; this was another problem which may at least in part be solved by training on site. Dr Hanson agreed that the way forward lay in supporting the development of local centres of excellence so that training at all levels could occur from within.

D. Specific techniques

Can ultrasound replace expensive contrast examinations?

Dr D. R. Naik

Dr Naik outlined some of the radiographic examinations which he believes can be replaced by the use of ultrasound. These include:

(a) for neonates and in paediatrics: congenital heart disorders, and renal tract and gastro-intestinal examinations;

(b) for adult patients: ultrasound as first line investigation of liver, renal tract and valvular heart disease and arterial and venous peripheral vascular disease.

He concluded that such procedures were safe, cheaper and better, a conclusion true for technically advanced as well as developing countries. Dr Naik stressed that he only recommended procedures which he used himself.

Low cost guided interventional procedures

Dr D. L. Cochlin

Dr Cochlin's essential point was that such procedures were expensive primarily because of the cost of the kits used for drainage and other procedures. He illustrated how tubes can be re-used and how guides can be made locally: the indispensable requirements were expertise and operator time.

Practical problems with isotope imaging

Dr W. I. Keyes

Dr Keyes first pointed out that "isotope imaging" is a "minority interest" and the "least important of the techniques being considered in this workshop". However, after this disclaimer, he then provided a detailed assessment of the usage of these techniques and practical advice on the requirements for an isotope imaging system set up in a developing country.

In the USA, these techniques represented 6% of all medical imaging, in the developing world perhaps 2% and in his own region, Cumbria, 4%.

Dr Keyes then set out the requirements for a basic radioisotope imaging system in order of priority:

Stable mains supply
Steady temperature
Supply of radionuclides and radiopharmaceuticals
Expertise
Room, say 4 x 4 m for the *in vivo* equipment.

A basic gamma camera can be a comparatively low cost device but, in addition to the initial capital cost, maintenance must be covered. Good cameras, now 5–10 years old, are available secondhand. Dr Keyes remarked, "A good man with a bad machine is better than a bad man with a good machine". He added that it was worth recalling that, in the UK and elsewhere, radioisotope techniques had often been introduced through radiotherapy departments, where there was already experience in dealing with radioactive materials for brachytherapy.

Film processing

Ms A. Paris

The performance of the film processing system was equally important to that of the X-ray machine. Incorrect processing is one reason for requiring a repeat radiograph. (Two films instead of one means twice the radiation dose.)

Environmental conditions were of great importance. Electricity for lighting (safelights) and temperature control of chemistry: water for mixing chemistry and for cleaning; good drainage to prevent pollution.

It was often difficult to buy, transport and store X-ray film. Simple training manuals on darkroom techniques and quality assurance testing were available from WHO, ISRRT, BIR and other bodies.

She stressed the need to keep processing simple, either using manual techniques or a simple automatic processor, with back-up spare parts and a code book to identify spares.

Discussion

Numerous points were raised on this group of papers:

(a) from experience, lowering of charges does increase the number of users of equipment;
(b) industry must be encouraged to provide good local back-up. Installation of an expensive CT system is useless if it is not maintained — and we know how costly that can be;
(c) training should relate to the work to be done at a particular site;
(d) to obtain and maintain good standards in radiography, first class supervision is the main tool.

E. Other perspectives

Difficulties in sending equipment to areas in need

Ms A. Paris

She outlined the problems as follows.

(a) The type of equipment to be provided — processing equipment, imaging equipment and all types of X-ray accessories. The items should be appropriate, acceptable and have a reasonable life span. Acceptability does depend on prospective usage; equipment must have a proven service record and the paperwork should be sent with the machine. We should note that needs can be very simple, *e. g.* lead letters.
(b) How does one send it? Personal contact; charitable foundation; specific trust.
(c) In planning: question the space available and services; expertise to install; suitable transport; official paperwork; associated costs.

The needs of radiographers/ X-ray technicians in developing countries

Miss M. Frank

Miss Frank spoke from her personal experience of over 30 years at The Middlesex Hospital School of Radiography which had trained over 300 radiographers from overseas countries in various types of tailor-made courses. In addition, she has been actively involved in the Education Committee of the ISRRT.

She said that it is difficult to evaluate training: what people do get from it is not what we think they should get. She summarized the main problems.

(a) Schools that train without reference to the available clinical facilities for the students to gain competence. Training must help the students to like the job and stay in it. Local economic, political and professional aspects must be understood. Many radiographers have to take a second job to make ends meet.

(b) There is generally a low morale among radiographers who need motivation, a realistic career structure and not to be treated as having a minor role in the imaging team.
(c) There is frequently a widespread and often muddled fear of radiation.
(d) There is a particular need for training in paediatric techniques, as children form a far higher proportion of the population.

WHO Technology discussions, now in progress, may help to solve some of these problems. The Commonwealth Foundation and the CEC have also been helping.

The concept of international "twinning" between medical centres

Mr J. Crawley

Mr Crawley considered that "high tech" procedures are valuable in monitoring the effectiveness of "low tech" methods used to deal with public health problems. Twinning, he said, needed to be informed and mutually accepted. From this country we can provide advice, software and spares. The recipient offers original projects and patients who would otherwise be untreated. Concerning equipment, surveys by IAEA showed that 30% of the equipment supplied was out of order. There were difficulties over spare parts, service personnel, test equipment and inadequate knowledge.

A form of twinning was under discussion in Vienna in 1986, but had proved difficult to implement in an informal manner within that organization.

Discussion

It was pointed out that modern equipment is generally more reliable, while for older equipment it is often easier to improvize repairs.

Dr D. E. Bechly thought that training should be modified where staff are expected to maintain equipment, but Miss Franck said that she found manufacturers were often unwilling to provide the "know-how" needed for maintenance.

F. Funds and resources

The role of the British Council

Dr D. J. Buchanan

British Council, London

(a) Outline of the Council's activities

Dr Buchanan explained that the British Council has representatives in 85 countries. Sixty per cent of the budget is spent on the exchange of people, 11% on specialized work in science and the rest on books and the arts.

Income is derived from a Government grant providing 35% of the costs, the Overseas Development Agency, 36%, and the Foreign and Commonwealth Office Agency, 6%. Direct revenue income is increasing, although the direct Government grant is in relative decline.

(b) Fellowships and other support

There are British Council Fellowships: decisions on these awards are made by the representative in the country concerned. Overseas training is provided, focused on poorer countries, for example in primary health care and agriculture. There is an increasing number of foreign and commonwealth scholars and support is also given by the Council of the European Communities (CEC). The council provides administrative arrangements for IAEA students in the UK. To anyone seeking support, the advice is to go to the Overseas Development Agency or to the Foreign and Commonwealth Office Agency first of all: the British Council will help through the local representative, who is the "point of contact".

British Council experience is that there is a considerable demand for training in the field of radiology. The type of training required varies from basic training in radiology and radiography to more specialized skill requirements in ultrasound, interventional radiology and aspects of radiotherapy. The British Council Medical Department is very keen to ensure that clinical training is of a high quality and has prepared a guidance note on what should be expected of a doctor in a supernumerary clinical training post.

Full details of support available through the British Council are provided in a leaflet entitled *Sources of Financial Assistance for Overseas Students* .

(c) Client funded studies

The British Council will help with communications, over testing for mastery of the English language and in providing a major information point on sources of support for overseas students.

Discussion

One speaker raised the problem of students wanting to change their course once they reached this country. Dr Buchanan said that he was well aware of this problem and that apart from the agreement entered into by the Fellow they also relied on the host organization alerting them when problems seemed to be arising.

Dr Hanson mentioned that WHO was collaborating with the development authorities in France, the University of Lyon and the University of the Ivory Coast to establish a Regional Radiology Training Centre to serve the French-speaking countries of Africa.

Part 2

Workshop Discussion and Conclusions

This part of the meeting sought answers, and possible consensus, on a set of specific questions.

(a) On what areas of expertise should attention best be focused (*e.g.* radiography, ultrasound)?

Here Dr Hanson (WHO) re-emphasized the importance of a referral structure in support of any primary health care and indicated that WHO advice will be to include both basic X-ray and ultrasound at primary referral level (when resources allow). He also emphasized however that it is only practicable to offer expertise in areas for which help has been requested locally. Often such locally expressed needs may differ from developed world preconceptions, with academic radiologists and health administrators feeling a major need for CT, and even MRI.

Endoscopy was suggested as a relatively "low-tech" area that could have substantial usefulness in support of primary care and where UK expertise might valuably be offered.

It was agreed that relative value of particular types of expertise could only properly be assessed in the context of a particular geographical centre or environment (see item (d) below) and knowledge of the corresponding health priorities.

(b) What types of support would be most effective?

Here again, it was agreed that the answer must depend on local need. Several areas were considered.

Training of radiologists, at various levels, is one clear need but this is already being addressed by RCR, both through its Middlemiss Fellowships and by collaborative workshop schemes, such as one recently initiated in India which included lectures, tutorials, film presentations and hands-on ultrasound experience.

Training of radiographers is also a major need but the point was again made here that it can only usefully be met where expression is given locally to such need.

Technical support was recognized as being a very great problem, and one to which BIR might be well suited to contribute, but one beset with difficulties: manufacturers will often contrive very effectively to protect their maintenance business but otherwise spares will be unavailable, trainee technicians will move over to TV servicing, and so on. No easy solution was suggested, but nor was there any lack of stories of unremedied equipment breakdown. However, IAEA is reported to be working on a scheme.

The value of bringing trainees to the UK was discussed. While this clearly can be valuable in some cases, several contraindications were identified: training may be carried out in unrealistic conditions, trainees may not return or, if they do, migrate to private practice.

Supply of books and journals (first or secondhand) was mentioned by several speakers as a highly cost-effective method of providing support.

Similarly, hard currency funding for support of young radiologists and other trainees to attend appropriate "Western" meetings was also suggested as being very worthwhile (particularly for Eastern Europeans).

(c) Should support initially be concentrated on one (or a few) sites?

Differing views were expressed here. WHO already encourages regional training centres (*e.g.* in Nairobi) and UK support of the right kind could be very effective there. The British Council also favours such schemes, of which at present there is even a dearth in relation to available funding.

Other speakers seemed to favour the concept of concentrating support but also suggested other candidates, such as Malaysia (where there is already a good record of training visits) and India.

Another view however, particularly expressed by Professor Isherwood, was that concentrating support on a too limited group of sites could be politically unacceptable, even if good in principle.

(d) What types and patterns of communication may be required?

As discussion moved towards establishing a co-ordinated UK resource structure there was support for the need to make known its existence to individuals who might make use of it, and thereby to identify and define specific needs. This could be through a combination of personal contact and announcements/advertisements in appropriate journals. As an example it was suggested that a BJR page could be used to solicit interest in co-ordinated assistance in addressing such questions as "What are your problems?", "How to deal with manufacturers, *e.g.* in ensuring proper maintenance", "What does a good radiograph/sonogram look like?". A recent announcement in *The American Journal of Roentgenology* was mentioned as an example here. Publications such as the RSM's *Tropical Medicine* are also relevant and valuable.

The further suggestion was made that the value of such a UK resource structure could be much enhanced if potential users (presumably major) could have access to it by funded provision of FAX.

(e) What sources of funding might be accessible for such a programme?

Dr Buchanan had previously indicated that British Council administered some funds, particularly under the Technical Co-operation Training Programme that is targeted partly at primary health care in Third World situations.

Otherwise, although no specific suggestions were put forward, it was generally agreed that a concerted UK approach to potential funding bodies, including trusts, could be very productive.

In relation to funding, however, Dr Hanson reported his experience that this, rather than the availability of suitable and willing volunteers (particularly the newly, or nearly, retired), is the rate-limiting factor in these activities.

(f) What co-ordination with existing bodies may be necessary or desirable?

It was clear that co-ordination with WHO would be vital and Dr Hanson's enthusiastic support of the meeting suggests that this will be able to occur.

Professor Isherwood had previously described the work of the Radiology Outreach Foundation (see above) and co-ordination will clearly be important here.

The names and functions of a number of other organizations with possible bearing on the subject were mentioned in discussion and it was agreed to assemble a list of these as an attachment to this report.

(g) Conclusions, and decisions on further action, including publication

The following steps for immediate action were agreed to be desirable.

(i) A meeting representative of the various UK radiological societies should be convened to consider setting up a UK co-ordination structure to address the suggestions arising from this workshop. This could include maintenance of a register of willing experts.

(ii) That representative meeting should be asked to consider the feasibility of setting up one or more expert topic groups to execute and co-ordinate practical action in particular areas.

(iii) A written record of the present workshop should be prepared and, following circulation to participants for comment, should if possible be published. *BJR* or *BIR Bulletin* would be suitable vehicles, but use of the text should be unrestricted.

(iv) The record of the workshop should include a list of relevant organizations and services.

Appendix 1
References and Bibliography

WHO, 1983. *A Radional Approach to Radiodiagnostic Investigations. Technical Report Series, 689* (World Health Organization, Geneva).

WHO, 1982. *Quality Assurance in Diagnostic Radiology* (World Health Organization, Geneva).

WHO, 1983. *Radiodiagnostic Manual for Practitioners: WHO Basic Radiological Service* (World Health Organization, Geneva).

WHO, 1985. *Future Use of New Imaging Technologies in Developing Countries* (World Health Organization, Geneva).

WHO, 1987. *Rational use of Diagnostic Imaging in Paediatrics. Technical Report Series, 757* (World Health Organization, Geneva).

Palmer, P. E. S., 1984. Appropriate technology for diagnostic imaging in small hospitals. *British Medical Journal, 288,* 1435–1437.

Palmer, P. E. S., 1985. Diagnostic imaging for develping countries. *WHO Chronicle, 39,* 143–148.

Quality Control Handbook (for technicians in radiography using simple X-ray equipment and manual film processing). Available from The Secretary General, ISRRT: Mr T. J. D. West, 52 Adison Crescent, Don Mills, Ontario, Canada M3B 1KB.

NRPB, 1990. Patient dose reduction in diagnostic radiology. *Documents of the NRPB, 1.*

Appendix 2
Relevant Organizations and Services

Equipment to Charity Hospitals Overseas ("ECHO": a trading charity), Ullswater Crescent, Coulsden, Surrey CR3 2HR.
Tel: 081-660 2220; Fax: 081-668 0751; Telex: 924507 ECHO G.
(Obtains ships and helps repair and maintain new and reconditioned medical equipment, spares and drugs.)

Ranfurly Library Service, 2 Coldharbour Place, 39 Coldharbour Lane, London SE5 9NR.
Tel: 071-733 3577.
(Acquires and organizes shipping of books to libraries etc. in developing coutries)

British Council, 10 Spring Gardens, London SW1A 2BN. Tel: 071-389 4215 (Medical Department).

Africa Educational Trust, 38 King Street, London WC2E 8JS.
Tel: 071-836 7940.

World Health Organization, Radiation Medicine Unit, CH 1211 Geneva 27, Switzerland.

Protekton Turst, 8 Kenilworth Gardens, London SE18 3JB.
Tel: 081-856 8477.
(Some limited funds to cover expenses of volunteer teaching of radiology/radiographic equipment, *e.g.* in Romania.)

Radiology Outreach Foundation, 3415 Sacramento Street, San Francisco, CA 94118, USA.

BIR Calendar

Unless otherwise indicated, enquiries about the following events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-580 4085).

Cerebral Blood Flow Practical Measurement and Clinical Relevance — a Multimodality Approach
February 12, 1991
All day Meeting
Organizer: Dr A. H. Smith
Chairmen: Dr D. A. Cunningham, Prof. B. S. Worthington and Dr R. A. Shields
Speakers: Prof. J. D. Pickard, Prof. M. A. Smith, Dr S. Padayachee, Prof. M. Levene, Miss D. Dorrance, Dr P. Butler, Dr J. N. H. Brunt, Dr K. E. Britton, Prof. P. J. Ell, Dr D. J. Wyper, Mr A. R. Naylor, Dr A. Lammertsma and Dr I. R. Moseley

Your CT Scanner — Are the Bells and Whistles Worthwhile?
February 20, 1991
All day meeting
Organizers: Drs A. Dixon and S. J. Golding
Speakers include: Dr H. J. Dobbs, Dr J. E. Adams, Dr K. Miles, Dr J. Gillespie, Mr A. D. Sant, Dr A. Dixon and Dr S. J. Golding

Radiobiology Proffered Papers
February 22, 1991
Organizer: Dr R. Camplejohn

Radiation Oncology/IPSM
April 10, 1991
All day meeting organized by IPSM

RADIOLOGY AND ONCOLOGY 91 and MED X RAY
29 April–1 May
Metropole Hotel, Brighton
Speakers:
3M Mayneord Memorial Lecture:
Prof. S. Dische
Silvanus Thompson Memorial Lecture:
Dr R. Berry
Presidential Address:
Prof. C. A. Joslin
Mackenzie Davidson Memorial Lecture:
Prof. S. Dische

Radiation Oncology and Radiobiology: Particle Therapy
June 7, 1991
Organizer: Dr R. D. Errington
Speakers: Dr D. Bewley, Dr N. McNally, Prof. G. W. Griffin, Mr J. Hungerford, Dr T. Bates, Dr S. Gore and Prof. J. M. Slater

The New Legislation — Friend or Foe (After the White Paper ... and into Europe)
June 13, 1991
All day meeting orginized by the Industry Committee
Chairmen: Prof. C. A. Joslin, Dr O. Craig and Miss D. Rigg
Speakers include Dr J. Roylance, Dr I. Watt, Mr E. Sutherland, Prof. I. Isherwood and Mr P. Richardson

Conversazione
June 27, 1991
Painter's Hall, London
Lecture: " Half an Eye on the Sky", by Sir Stephen Furness.

Is there a seminar, conference or evening get-together you want to organize, but you don't have the time? The BIR Conference Office may be able to help you. Please call Vanessa Whitehead, Conference Manager, to discuss possibilities.

Lecture, Conference and Meeting Facilities

Available for use at 36 Portland Place, London W1

The BIR lecture Theatre, with raked seating and extensive audiovisual equipment, accomodates 100 people in air conditioned comfort.

The conference room accommodates a maximum of 34 people with modular furniture which can be arranged to suit the needs of individual users.

For further information please contact the House Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

Library News

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays and Thursdays).

The journal stock includes more than 100 titles. Although journals may not be taken out of the library, there is a photocopy service, also available by post or Fax. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

Members can apply to the BIR librarian for a visitor's card which allows limited use of the RSM library for reference purposes, including photocopying and searches.

Recent aquisitions

IAEA, 1989. Principles for the establishment of upper bounds to doses to individuals from global and regional sources.

MARTINEZ, A. A., ORTON, C. G. & MOULD, R. R. (Eds), 1989. Brachytherapy HDR and LDR. Proceedings: Brachytherapy Meeting: Remote Afterloading: State of the art, May 1989.

New BIR Members

Medical

Prof Dr Edward Baral, MD, PhD
(Canada), Radiotherapist/Oncologist
Dr Martin J. K. Blomley, MA, MRCP, MB, BS
(London), Diagnostic Radiologist
Dr Paul Butler, MRCP, FRCR
(London), Diagnostic Radiologist
Dr Anna Maria Cassoni, BSc, MB, BS, MRCP, FRCR
(London), Radiotherapist/Oncologist
Dr Shailendra Chopra, MB, BS, MD (Radiodiagnosis)
(London), Diagnostic Radiologist
Dr John F. Cockburn, MB, BCh, BAO, MRCP
(London), Diagnostic Radiologist
Dr Roger D. Errington, BSc, LRCP, MRCS, MB, BS, DCH, DMRT, FRCR
(Wirral), Radiotherpist/Oncologist
Dr Thomas Fitzgerald, MB, ChB, FRCR
(Fife), Diagnostic Radiologist
Dr Fergus V. Gleeson, MB, BS, MRCP, FRCR
(London), Diagnostic Radiologist
Dr Maria Grossmann, MD, LRCP, MRCS, DMRE
(London), Diagnostic Radiologist
Dr Jeremiah C. Healy, MB, BChir, MA, MRCP
(London), Diagnostic Radiologist
Dr Nancy D. Jonker, DCR, MB, ChB
(London), Diagnostic Radiologist
Dr David Kessel, MRCP
(London), Diagnostic Radiologist
Dr Ann D. King, MB, ChB, MRCP
(London), Diagnostic Radiologist
Dr Martin J. Lipton, MD
(USA), Diagnostic Radiologist
Miss Jessie MacLellan, BA, MA
(Woodford Green, Essex), Psychologist
Dr Marian O'Reilly, MB, BCH, BAO, MSc, MRCPI, DCH, BEd
(London), Diagnostic Radiologist
Dr Pat Price, MA, MRCP, FRCR
(London), Radiotherapist/Oncologist
Dr Gareth J. G. Rees
(Bristol), Radiotherapist/Oncologist
Dr John I. S. Rees, MB, BCh, BSc, FRCR
(Cardiff), Diagnostic Radiologist
Dr David A. T. Silver, MB, BS, BSc, MRCP
(Bristol), Diagnostic Radiologist
Dr Thomas M. Snow, BSc, BM, BCh, MRCP
(Bristol), Diagnostic Radiologist
Dr Pieter L. M. van de Voort, Radiologist
(Netherlands), Diagnostic Radiologist
Dr Sarah J. Vinnicombe, MB, BS, BSc, MRCP
(London), Diagnostic Radiologist
Dr Joseph Wee, MB, BS, FRCR (Part I)
(London), Radiotherapist/Oncologist

Non-Medical

Dr Peter Almond, PhD (Medical Physics)
(USA), Physicist
Mr Clive Baldock, MSc, BSc
(London), Physicist
Mr Jonathan Betser, Diploma in Osteopathy
(Dunstable, Beds)
Mr Richard P. Cannon, HDCR
(London), Radiographer
Miss Claire-Louise Chapple, BA, MSC
(Newcastle upon Tyne), Physicist
Mrs Cynthia Copping, BSc, MSc
(Lincoln), Physicist
Mr Stephen J. Duck, BSc, MSc
(Wirral, Merseyside), Physicist
Mr Ingvar A. J. Fife, DCR(R), BSc, MSc
(London), Physicist
Mr Orphan A Hachinene, MSc, PGD, Dip Physics, DTE, DDR
(Zambia), Physicist
Mr Steven Lawson, DCRR, DRI
(Swindon, Wilts), Radiographer
Mr Alastair S. McEwan, CA, BCom
(Edinburgh), Managing Director
Mr Jack Riley, Director of Purchasing
(USA), American Medical Ltd
Mr Peter J. Sharpe, DCR, DMS
(Taunton, Somerset), Radiographer
Mr Barry White
(Sunbury on(Thames), Siemens PLC

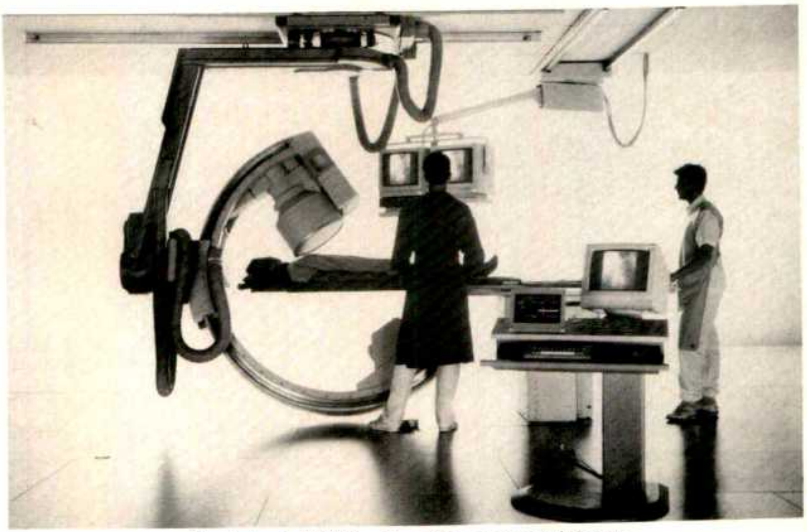
Industry News

Integris V 3000

Based on the latest Philips' technology of parallel processing, the Integris V 3000 is dedicated to all vascular and interventional X-ray procedures. All major system units are furnished with autonomous intelligence for internal control and communication with other segments. The system allows multimode digital acquisition, including digital subtraction angiography, digital peripheral angiography and digital radiography as standard modes.

The Integris V 3000 is equipped with the award-winning ceiling suspended C-arm. The positions of the arm can be stored and recalled with the Auto Position Controller. The floating and motorized tabletop has a large reach and provides excellent patient coverage, in particular for peripheral studies.

For further information contact Dr S. A. van Meurs, Philips Medical Systems, P. O. Box 10000, 5680 DA Best, The Netherlands.



The Integris V3000 with ceiling suspended C-arm

Colour Doppler function for endovaginal probe

Toshiba Medical Systems has recently introduced a special endovaginal colour package for the SSA-270A ultrasound scanner. The colour package will be exhibited at the 1st International Conference on Ultrasound in Obstetrics and Gynaecology, which is being held in London, 7–10 January, 1991.

Using this package, colour Doppler examinations can be performed with the existing PVE-582V 5.0MHz endovaginal probe. This colour package can be used by current owners of a SSA-270A with PVE-582V.

The high colour sensitivity of Toshiba's new endovaginal probe makes it possible to detect tumour vascularization in a very early stage. Many other applications are also possible.

For more information please contact Toshiba Medical Systems Europe, SP/PR department, Schieweg 1, 2627 AN Delft, The Netherlands. Tel: 31 15 610121. Fax: 31 15 622359.

Radiological voice system

California Medical Software Inc recently unveiled their radiology reporting system at the US Embassy's Medical Matchmaker.

The Radiological Voice System II uses voice recognition technology to generate complete radiology reports in less than a minute. This is accomplished by the use of "voice-text" macros which are pre-defined words, phrases, sentences and paragraphs that are linked together to construct reports. Completely normal reports are generated by the utterance of as few as 2–3 words.

When one considers that between 75 and 80% of all radiology studies are normal, the RVS2 can be used to reduce the turn around time for the dictation and transcription of reports. By limiting the need for secretarial resources it reduces overall departmental costs.

The relational database on which the system is built allows all reports to be entered, reported on, saved and retrieved in the same manner as commercial business databases. The program operates in DOS, Unix and Xenix environments and can be linked to mainframes, used in a Local Area Network or as a standalone system.

For further information please contact California Medical Software Inc, 6347 Wynne Avenue, Suite 109, Reseda, CA 91335-7065, USA. Tel: 818 609 7466. Fax: 818 609 9026.

CT accessory for use with the Ximatron Simulator

Varian Medical Equipment has revealed a computer tomography accessory system which will improve radiation planning for cancer patients by allowing CT scanning and simulation on the same machine. This option has already been used to scan nearly 200 patients at its first clinical test side in Australia.

Immediately after simulation, with the patient still in the final setup position, an operator can take a series of CT slices. This is done by inserting a filter into the simulator accessory mount, attaching a collimator to the image intensifier, then switching to the CT mode on the Ximatron's operator console. With a specially built camera and Varian proprietary algorithms, the Ximatron/CT Option has superior resolution and image display.

The Royal North Shore Hospital in Sydney, Australia has been using the Ximatron/CT Option for the past year. It will be at beta test sites in 1991. Varian anticipates its release as a product in the first quarter of 1992.

For more information please contact Varian International AG, Medical Equipment, Kollerstrasse 38, CH-6300 Zug, Switzerland.

Radiology computer "up and running" at St Georges

On 1st November Dr John Williams, Director of Radiology at St George's Hospital, London, officially accepted the Radiology Department's new Computer System. The system went "live" on 1st October and has already processed the details of over 10,000 examinations.

The System installed is the Network Radiology Management System from Agfa-Gevaert Ltd and Amersham Medical Systems. The 26 terminals and associated printers and bar code readers are networked via an extensive Ethernet and Fibre Optic Cable complex to all the main imaging departments, providing administrative and managerial support for one of the busiest radiology departments in London.

The RMS System is a multi-user, multi-tasking computer network with application software developed specifically for the UK medical environment and uses advanced computer hardware including laser printer and colour screens. This system is one of the most comprehensive radiology information management networks in the country.

Dr Williams accepted the system from Grahame Mountford, Divisional Director of Diagnostic Imaging Systems, Agfa Gevaert.

MICRO AM from Kontron

Kontron Instrument's MICRO AM is a small device which combines auscultatory and oscillometric ambulatory blood pressure measurement with advanced real-time ECG analysis for editable arrhythmia and 2-channel ST level and slope recording. The three measurement modalities are synergistic and mutually validating, enabling artefact-free blood pressures to be measured on request and during ECG events. Summary, tabular and graphic reports are generated via the MICRO AM printer system.

For further details please contact Drew Mowatt, Kontron Instruments, Blackmoor Lane, Croxley Centre, Watford, Herts WD1 8XQ.
Tel: 0923 245991.

Platinum ultrasound from Philips

Philip's Platinum ultrasound system was on display at the BMUS meeting during December. It offers numerous innovations based on its electronics, computer architecture and ergonomic design.

Features of the system include colour velocity imaging (CVI) which has been designed to overcome the limitations of colour Doppler processing and present a more complete and accurate depiction of blood flow, and variable focal windowing which allows the operator to expand or compress one to twelve focal zones as small as 1 cm or as deep as the entire imaging field, to detect smaller pathologies.

Platinum's award-winning design is suitable for a wide range of applications: adult and paediatric abdomen, cerebrovascular and peripheral vascular, neonatal brain, small parts, high risk obstetrics and gynaecology.

MRI package from Wardray and DC Bayman Construction Ltd

Wardray and DC Bayman Construction Ltd have pooled their resources to design a complete package for MRI facilities. This can include all related building, electrical and decorating work plus an entirely British manufactured magnetic resonance shielding system.

All individual side requirements can be achieved in the building of a rigid, self-supporting structure providing an attenuation exceeding 100db at 100MHz. Rooms, in addition to doors with a high quality locking mechanism, can include windows, filters, penetration support panels, access panels for maintenance, and flush floor cable ducting.

For further information contact Wardray Products Ltd, Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP.
Tel: 081-398 9911.

Baritop products and Bioglan Effervescent Granules

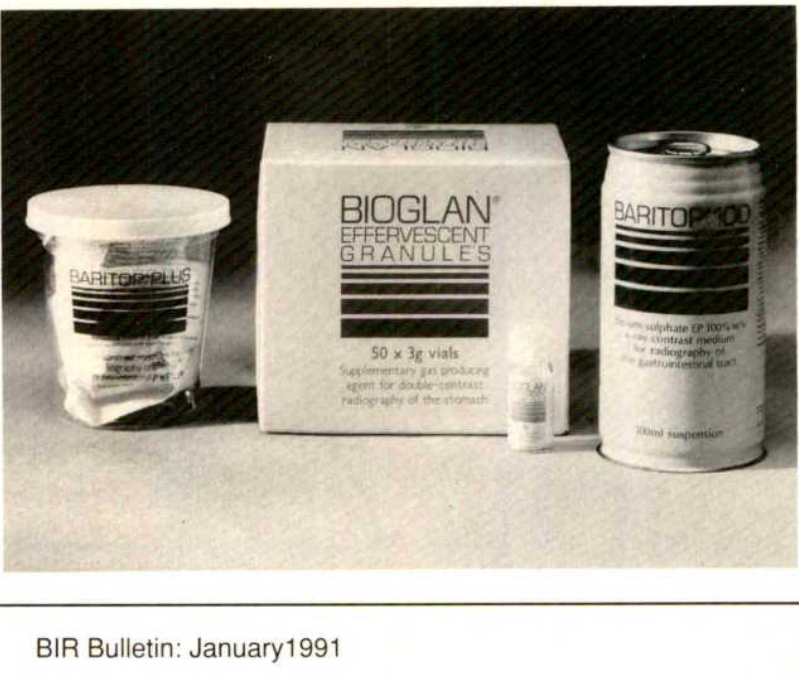
The repackaging of Bioglan's diagnostic range has now been completed and supplies of updated product are available as follows.

Baritop Plus: a hermetically sealed "tamper evident" sachet containing fine white granules of barium sulphate, with no added flavour for use as an X-ray contrast medium for radiography of the gastrointestinal tract.

Bioglan Effervescent Granules: "ready to use" vials of dust free, fine white granules, for use as a supplementary gas-producing agent for double-contrast radiography of the stomach.

Baritop 100: a unique product presented in a ring-pull can containing a white pleasant-tasting suspension of Barium sulphate EP 100% w/v, with carbon dioxide as an effervescent agent. Baritop 100 is designed for double-contrast radiography and used as an X-ray contrast medium for the gastrointestinal tract.

Further information is available from: Bioglan Laboratories Ltd, 1 The Cam Centre, Wilbury Way, Hitchin, Hertfordshire SG4 OTW. Tel: 0462 438444.



BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £275 p.a. member companies are offered an attractive benefits package.

To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex
TW8 9AX.
Tel. 081-560 2131. Product Areas 1. Contact Mr G. Mountford, Director.

American Medical Ltd
PO Box 971, London SW10.
Tel. 071-352 8051. Fax: 071-376 4508.
Product areas 1, 3, 4, 5, 7, 8.
Contact Betsy Riley, Managing Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury,
Bucks HP20 2TP.
Tel. 0296 395222.
Product areas 4, 5, 6.
Contact Mr James McLaughlin, Sales and Marketing Manager.

Bard Ltd
Forest Houe, Brighton Road, Crawley,
West Sussex RH 11 9BP.
Tel. 0293 27888, ext. 2204.
Product area 2.
Contact Anna Shores, Product Manager.

British Nuclear Fuels plc
Room 525, Hinton House, Risley, Warrington, Cheshire WA3 6AS.
Tel. 0925 835022.
Product areas 8, 11. Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Bruel & Kjaer (UK) Ltd
92 Uxbridge Road, Harrow, Middlesex,
HA3 6BZ.
Tel. 081-954 2366.
Product areas 3, 6.
Contatct Mr Dennis Lewis, Sales Manager.

Cardiac Services Ltd
95A Finaghy Road, South Belfast BT10
OBY. Tel. 0232-625566.
Product areas 1, 3, 4, 5, 6.
Contact Mr R. J. Brown. Managing Director.

Cea (UK) Ltd
Nissen House, Grovesbury Road,
Leighton Buzzard, Bedfordshire
LU7 8SS.
Tel. 0525 382529. Fax: 0525 372619.
Product areas 1, 3, 4, 5, 6.
Contact John Dunster, Managing Director.

Du Pont (UK) Ltd
Wedgwood Way, Stevenage, Hertfordshire SG1 4QN. Tel. 0438 734000.
Product areas 1, 3, 4, 5, 6, 7, 9 and 10.
Contact Mr E. G. Lovat, Product Manager, Diagnostic Imaging.

E. G. & G. Limited
Vale Road, Windsor, Berkshire SL4 5JP.
Tel. 0753 855611.
Product areas 1, 6, 7, 8.
Contact Miss Susan Holgate, Sales Executive (Therapy).

Elscint (GB) Ltd
Colonial Business Park, Colonial Way,
Watford, Herts WD2 4PT.
Tel. 0923 39511.
Product areas 1, 3, 4.
Contact Faith Gorman, Marketing Manager.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20.
Tel. 081-446 9714.
Product areas 1, 2, 8.
Contact Richard Bayliss, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London
NW3 6JH. Tel. 071-586 9351.
Product areas 1, 3.
Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
34 Shakespeare Street, Nottingham
NG1 4FQ. Tel. 0602 483807.
Product areas 1, 3, 4, 5, 6.
Contact Miss Eileen Parr, Commercial Manager.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks
SL1 4ER. Tel. 0753 874000.
Product areas 1, 2, 3, 4, 5, 6, 8, 9.
Contact Jill Mitchell, UK Sales Support.

Kodak Ltd
PO Box 66, Station Road, Hemel
Hempstead, Herts HP1 1JU.
Tel. 0442 61122.
Product area 1.
Contact Mr P. E. Blackwell, Manager, Health Sciences Division.

Lanmark
PO Box 317, Beaconsfield, Bucks
HP9 2LR.
Tel. 0494 791615/670586.
Product areas 1, 3, 4, 5, 9, 10, 15, 16.
Contact Liz Beckmann, Director.

3M UK PLC
3M House, Bracknell, PO Box 1,
Berks RG12 1JU.
Tel. 0344 426726.
Product area 1.
Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney, Northampton NN3 4RQ.
Tel. 0604-46132.
Product areas 4, 5.
Contact Mr D. G. L. Wood, Business Manager.

M. A. S. Medical Ltd
Armytage Road, Brighouse, West Yorkshire HD6 1QF. Tel. 0484 721906.
Contact Martin York, Managing Director.

Merit Health Systems Ltd
1 Viking Close, Great Gutter Lane, Willerby, North Humberside HU10 6DZ.
Tel. 0482 652252.
Product area 13.
Contact Mr W. Blakemore, Director.

Medical Xray Supplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU. Tel. 081-205 9500.
Product area 1.
Contact Mr R. J. Laird, Sales Director/Mr K. Wartnaby, Managing Director.

Mitsubishi Electric UK Ltd
Travellers Lane, Hatfield, Herts AL10 8XB.
Tel. 07072 78756.
Product area 14.
Contact T. F. McCloud, Sales and Marketing Manager.

National Power plc
14 Newgate Street, London EC1A 7AM.
Tel: 071-634 6898.
Product areas 7, 8.
Contact Mr A. J. Swanson, Assistant Company Secretary.

Nuclear Associates
100 Voice Road, Carle Place, New York 11514-1593, USA.
Tel. 516-741 7614.
Product areas 1, 3, 4, 5, 6, 8.
Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd
Nucletron House, Tarporley Business Centre, Tarporley, Cheshire, CW6 9UY.
Tel: 0829 733611.
Product areas 6, 8.
Contact Mrs Marilyn A. Hart, Office Manager.

Nycomed (UK) Ltd
Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA. Tel. 021-742 2444.
Product areas 1, 3.
Contact Mr L. Birch Hansen, Managing Director.

Oxford Magnet Technology
Wharf Road, Eynsham, Oxford.
Tel. 0865 880880.
Product area 1.
Contact Pauline Hobday, Director of Sales and Marketing.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ. Tel. 081-741 1666.
Product areas 1, 3–8.
Contact J. M. Woolston, Sales and Marketing Manager.

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1st UAE Diagnostic Radiology and Imaging Conference
January 14–17, 1991
Abu Dhabi, United Arab Emirates
Further details: Dr Abdul Rahim Jaafar, Chairman, Organizing Committee, Assistant Under-Secretary, Ministry of Health, Mafraq Hospital, PO Box 2951, Abu Dhabi, UAE. Fax: 21549.

Diagnostic Radiology in Aruba
January 20–26, 1991
Aruba
Further details: Radiology Postgraduate Education Office, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, USA. Tel: (212) 746 2522.

Personal Dosimetry — Present and Future
January 22, 1991
London
Further details: Dr D. N. S. Dixon, Programme Committee Secretary, The Society for Radiological Protection, 67 Oatlands Park, Linlithgow, West Lothian EH49 6AS. Tel: 031-244 2779.

Advances in the Treatment of Myocardial Infarction
January 24–25, 1991
London
Further details: Catherine Barrett, IBC Technical Services, Bath House, 56 Holborn Viaduct, London EC1A 2EX. Tel: 071-236 4080. Fax: 071-489 0849.

Computed Body Tomography 1991 — The Cutting Edge
February 7–10, 1991
Florida, USA
Further details: Program Coordinator,The Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205, USA. Tel: (301) 955-2959.

Clinical Aspects and Modern Management of Lung Disease
February 12–13, 1991
London
Further details: Georgina Mason, IBC Technical Services, Bath House, 56 Holborn Viaduct, London EC1A 2EX. Tel: 071-236 4080. Fax: 071-489 0849.

Principles and Practice of Clinical MRI
February 28–March 5, 1991
Florida, USA
Further details: Program Coordinator,The Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205, USA. Tel: (301) 955-2959.

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April 1–13, 1991
Munich, FRG
Further details: GSF Kongressdienst, Ingolstädter Landstrasse 1, D-8042 Neuherberg, Federal Republic of Germany. Tel: (089) 31872669; Fax: (089) 31873362.

The 1991 International Symposium on Radon and Radon Reduction Technology. "A New Decade of Progress"
April 2–5, 1991
Philadelphia, USA
Further details: Pat Heightchew, CRCPD, 205 Capital Avenue, Frankfort, KY 40601, USA. Fax: (502) 227-7862.

Fundamentals of Medical Ultrasonics
April 17–19, 1991
London
Further details: Mr K. N. Humphries, Wolfson Conference Centre, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0NN. Tel: 081-743 2030 Ext 2210.

Advances in Hip and Knee Arthroplasty
April 25–27, 1991
Virginia, USA
Further details: Conference Coordinator, The Johns Hopkins Medical Institutions Office of Continuing Education, Turner 20, 720 Rutland Avenue, Baltimore, MD 21205-2195. Tel: (301) 955-2959.

Radiology and Oncology 91
April 29–May 1, 1991
Brighton
Further details: The Conference Office, The British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

Contrast-Enhanced of Magnetic Resonance
May 23–25, 1991
California, USA
Further details: Society of Magneticl Resonance in Medicine, 1918 University Avenue, Suite 3C, Berkeley, CA 94704, USA. Tel: (415) 841-1899. Fax: (415) 841-2340.

33rd Annual Meeting of the International College of Angiology
June, 1991
Singapore
Further details: Denise M Rossignol, International College of Angiology, 1044 Northern Boulevard, Ste. 103, Roslyn, New York 11576, USA. Tel: (516) 484-6880. Fax: (516) 625-1174.

Tenth Annual Scientific Meeting and Exhibition
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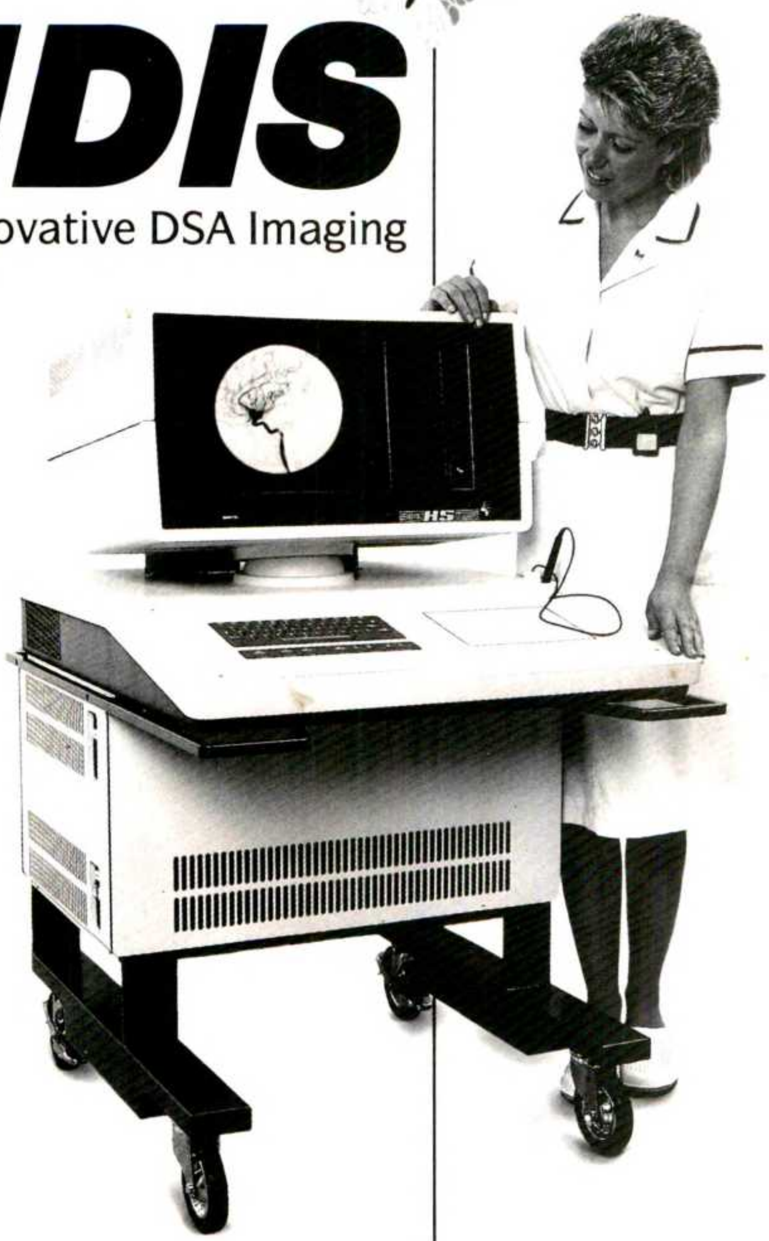

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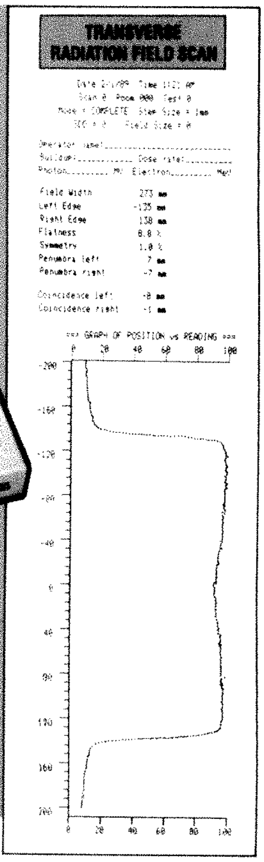

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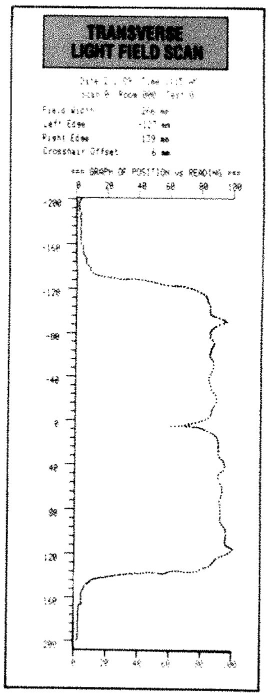

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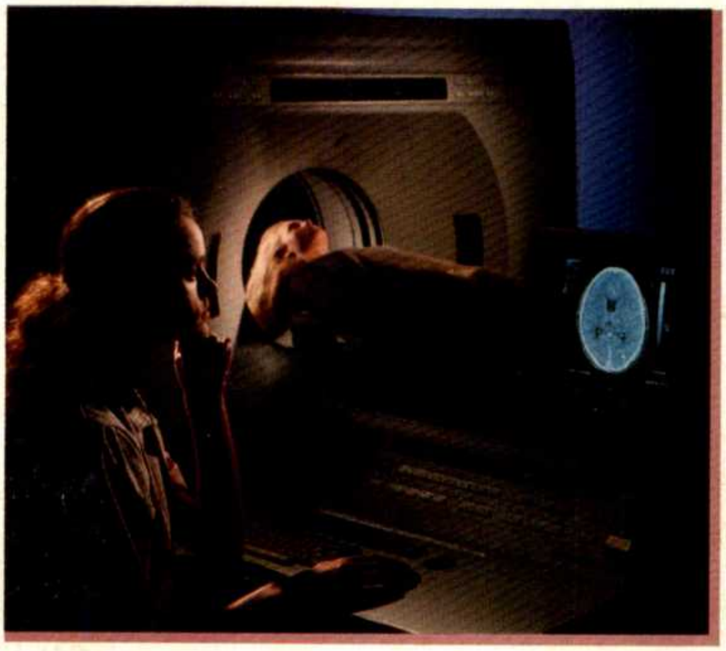

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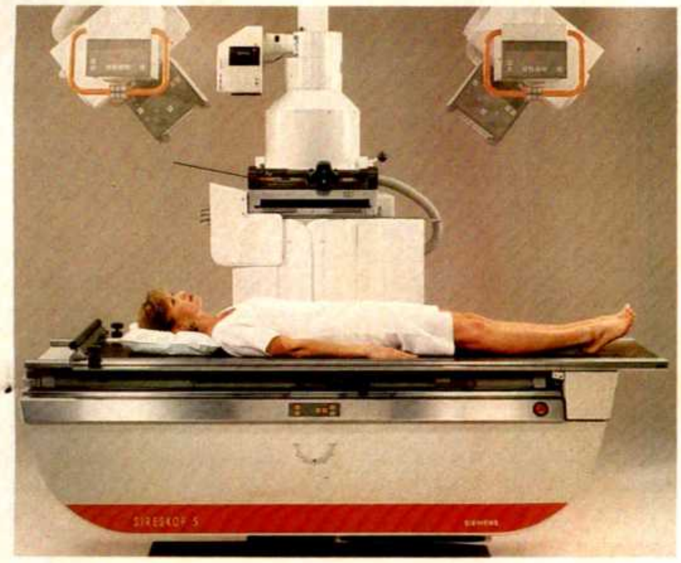

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The British Journal of Radiology

Observation of cerebrospinal fluid flow with echo-planar magnetic resonance imaging

By M. K. Stehling, MD, PhD, *J. L. Firth, FRCS, †B. S. Worthington, BSc, D. N. Guilfoyle, PhD, R. J. Ordidge, PhD, R. Coxon, PhD, A. M. Blamire, BSc, P. Gibbs, BSc, *P. Bullock, FRCS and P. Mansfield, PhD, FRS

Department of Physics, University of Nottingham and Departments of *Neurosurgery and †Academic Radiology, Queen's Medical Centre, Nottingham NG7 2RD, UK

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Keywords: Echo-planar magnetic resonance imaging, Cerebrospinal fluid

Abstract. Using echo-planar (EP) magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) flow patterns have been demonstrated in the normal subject and patients with pathological conditions including communicating hydrocephalus, aqueduct stenosis and syringohydromyelia. Snap-shot imaging times of 128 ms allow detailed demonstration of transient intraventricular CSF flow patterns, which is not possible with conventional MRI. The potential of EPI as a method for qualitative and quantitative assessment of CSF dynamics is illustrated.

A number of different approaches have been made using conventional two-dimensional Fourier transform magnetic resonance imaging (2D-FT MRI) techniques to image cerebrospinal fluid flow within the ventricular system and basal cisterns (Bergstrand et al, 1985; Bradley et al, 1986; Jolesz et al, 1987). Superimposed on the slow overall circulation of cerebrospinal fluid (CSF) are respiratory and cardiac dependent pulsatile flow which can be identified on MR imaging by "time of flight" effects (Singer, 1978) as well as reversible and irreversible phase changes (Wehrli et al, 1984). Conventional MRI techniques, however, employ repetitive data acquisition over an extended period of time so that flow patterns can only be depicted as a weighted average over time. Even when time-resolved flow information has been obtained by means of cardiac gating, only regular and repetitive features of flow are captured and information about transient flow patterns is lost. The requirements for an ideal method of studying CSF flow *in vivo* would include the following: first, it should be non-invasive; secondly have no planar restrictions; thirdly be capable of gathering data very rapidly; and finally provide directional information and quantification of flow over the full range of values found in normal subjects and pathological conditions.

Echo-planar imaging (EPI) is an ultrafast nuclear magnetic resonance technique able to produce snap-shot images in typically 30–100 ms (Mansfield, 1977). We have applied EPI operating in a real-time mode to observe CSF dynamics in the normal subject and several patients with pathological conditions including hydrocephalus and syringohydromyelia. The first observations of CSF flow by EPI and attempts to quantify slow flow have been reported previously (Mansfield et al, 1986; Howseman et al, 1987). The ability to depict CSF signal intensity changes with EPI allows demonstration of CSF flow phenomena with high spatial and temporal resolution. This allows a detailed description of individual flow patterns and their evolution in time.

The simulation of flow phenomena in phantoms provides a basis for qualitative interpretation of the CSF flow patterns which are observed *in vivo*.

Technique

Imaging was carried out on our home-built 0.52 Tesla EPI scanner. An actively shielded whole-body gradient coil system was used in conjunction with a purpose-built head-size birdcage RF coil.

The pulse sequence and *k*-space diagrams in Fig. 1 show how an EP image is acquired. The rapidly switched frequency encoding *y*-gradient creates 128 gradient echoes in 128 ms. Each gradient echo corresponds to one of the 128 lines in *k*-space. Phase encoding is obtained through *x*-gradient bursts (blips) at the *y*-gradient zero-crossings. Full details of the modulus blipped echo-planar single shot technique (MBEST) as used for transaxial scanning is given elsewhere (Howseman et al, 1988; Ordidge et al, 1988; Stehling et al, 1989).

For imaging in the coronal and sagittal planes, the

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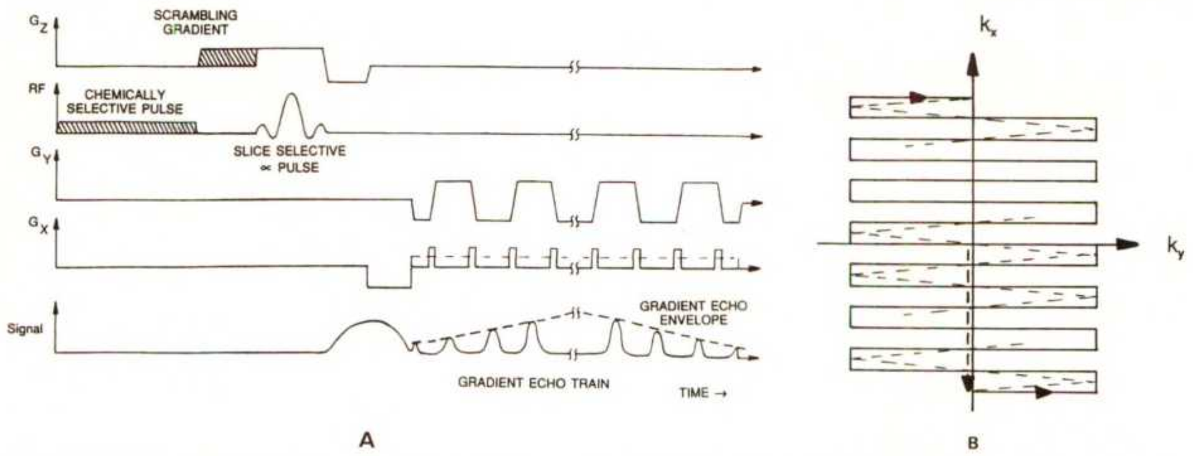

Figure 1. MBEST and EPI (dashed) pulse sequence diagram (A) and *k*-space trajectories (B). For coronal plane EPI, the rapidly switched frequency encoding gradient is along the *y*-axis, while for sagittal EPI it is along the *x*-axis. The chemically selective phase (shaded) provides lipid/water proton signal suppression when required.

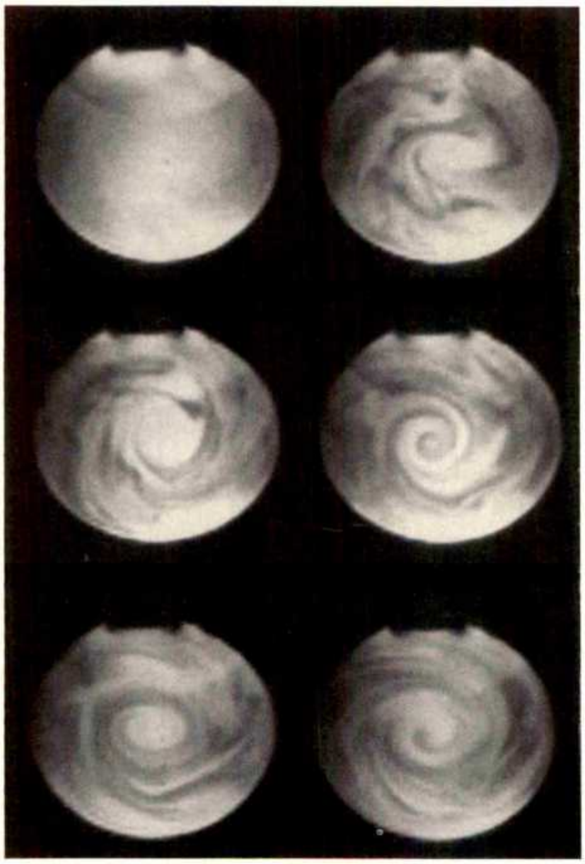

Figure 2. Six consecutive 64 ms MBEST snap-shots of circular flow in a 20 cm diameter water phantom. Dark areas indicate partially saturated spins (TR ≈ 620 ms), moving within the image plane. In the first image of the sequence (TR $= \infty$) flow, although present, is not detected. Bright areas are caused by flow components perpendicular to the image plane, resulting in flow related enhancement.

slice selective gradient is applied along the *x*-axis and the *y*-axis respectively. The extent of the imaging plane along the *z*-axis is defined by the sensitive volume of the RF coil. This provides a reasonably sharp cut-off which avoids aliasing in the *z*-direction. Slice selection is followed by a standard EPI pulse sequence (Mansfield, 1977). This employs a non-blipped phase encoding gradient and creates the zig-zag *k*-space trajectory shown dashed in Fig. 1B. The constant low level phase encoding gradient was necessary in this case because the high inductance of the *z*-gradient coil prevented application of the *z*-gradient blips. All images are based on 128×128 pixel arrays with approximately 1.7 mm in-plane resolution and a slice thickness of 10 mm. Acquisition of a complete two-dimensional EP image takes 128 ms.

For the creation of movie loops, triggered image acquisition was employed with 16 progessively delayed steps through the cardiac cycle triggered from a peripheral pulse monitor. The repetition time (TR) delay between consecutive frames was of the order of 2 s which allowed almost complete T_1 relaxation of brain tissue between shots. CSF proton spins were partially saturated and thus sensitized to flow through the imaging plane.

Grey–white matter contrast in MBEST and EP images is based on the intrinsic T_2-weighting of these techniques, caused by the delayed signal maximum of the echo-train (for full explanation see the following: Howseman et al, 1988; Ordidge et al, 1988; Stehling et al, 1989). To a first approximation the contrast in the MBEST images shown here is equivalent to that provided by a 3000/63 spin echo sequence.

Results

Flow phantoms

To verify the theoretical flow dependency of EPI two different phantoms were used to demonstrate the effects of bulk flow in EPI images.

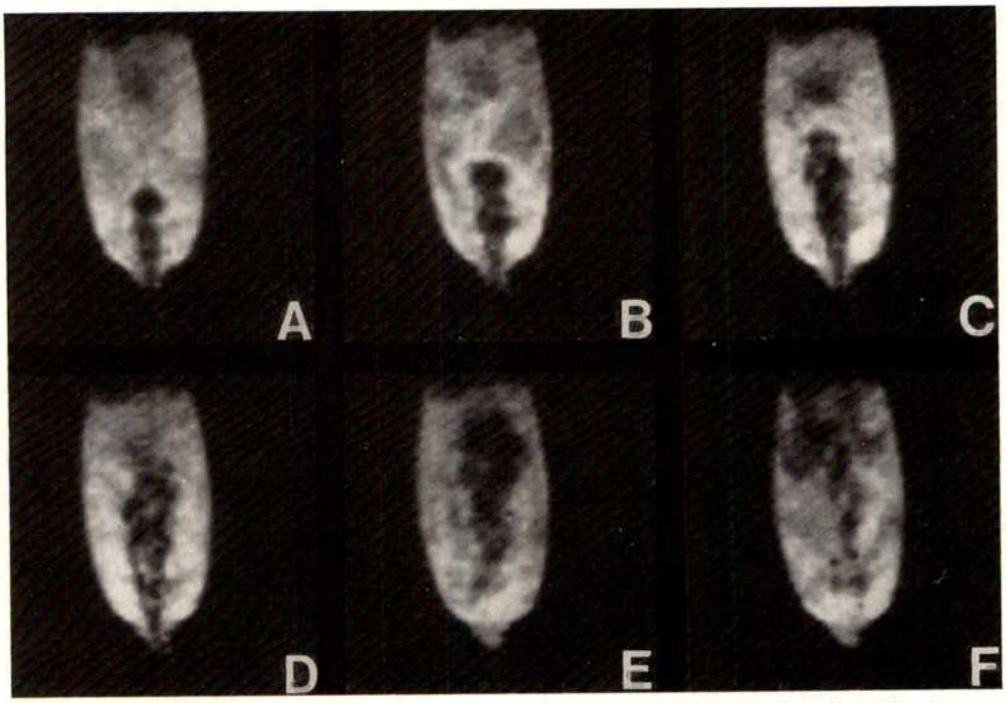

Figure 3. Six 64 ms MBEST images demonstrating signal dephasing caused by turbulent in-plane flow. The flow patterns were induced by squirting 1 ml of water through a narrow nozzle into 150 ml of stagnant water.

Flow into the imaging plane was produced with the "swirling water" phantom. A simple cylindrical 20 cm diameter plastic bottle filled with tap water was spun about its longitudinal axis to establish circular flow and the contents of the bottle were then imaged. The eight 64 ms MBEST images shown in Fig. 2 were acquired with a TR of 620 ms between consecutive images. The maximum linear flow velocity at the perimeter of the bottle was approximately 30 cm/s. The high signal intensity spiral patterns in images 2–8 are caused by the introduction of fresh spins into the imaging plane by the component of flow perpendicular to it. These newly added spins provide an indication of the in-plane component of the flow. The absence of flow patterns in the first image, with flow already established but no preceding excitation, clearly indicates the T_1 relaxation based nature of this phenomenon.

Rapid in-plane flow was demonstrated with a phantom composed of two 150 ml plastic bottles connected by a 2 mm bore plastic tube. Approximately 1 ml of water was gently squeezed through the plastic tube from one bottle into the stagnant water of the bottle depicted in the images in Fig. 3. Images were obtained with incremental time delays after squeezing and show the development of a jet originating from the small nozzle at the end of the connecting tube. Turbulent flow within the jet causes spin dephasing and results in a signal void. Note the detailed patterns of turbulent flow in the upper part of the phantom.

CSF flow

A representative series of coronal images from a normal volunteer is shown in Fig. 4. These were taken through a single plane intersecting the cerebral hemispheres, brainstem and upper cervical cord. The CSF within the ventricular system, basal cisterns and subarachnoid pool around the cord appears bright. Sequential images triggered to the cardiac cycle show that in systole the signal form from the CSF at the foramen magnum disappears, indicating rapid CSF flow between the intracranial and intraspinal compartments. Pulsation of CSF within the cervical theca and basal cisterns is a phenomenon which was well known to neuroradiologists when carrying out Myodil myelography and cisternography (Du Boulay, 1966). This is strikingly displayed on the movie loop and with improvements in spatial resolution pulsatile movement of the brain parenchyma should be detectable. Evidence for vascular pulsation based brain motion has recently been demonstrated by MR velocity imaging (Feinberg & Mark, 1987).

Complex flow patterns within the ventricles have been demonstrated in a patient with aqueduct stenosis.

Figure 5 shows a movie loop of 16 coronal 128 ms acquisition time EP images 2 cm posterior to the foramina of Monro. Areas of high signal intensity are seen within the lateral ventricles which wax and wane. Peripheral to these are irregular bands of low signal intensity. The former represent flow perpendicular to the imaging

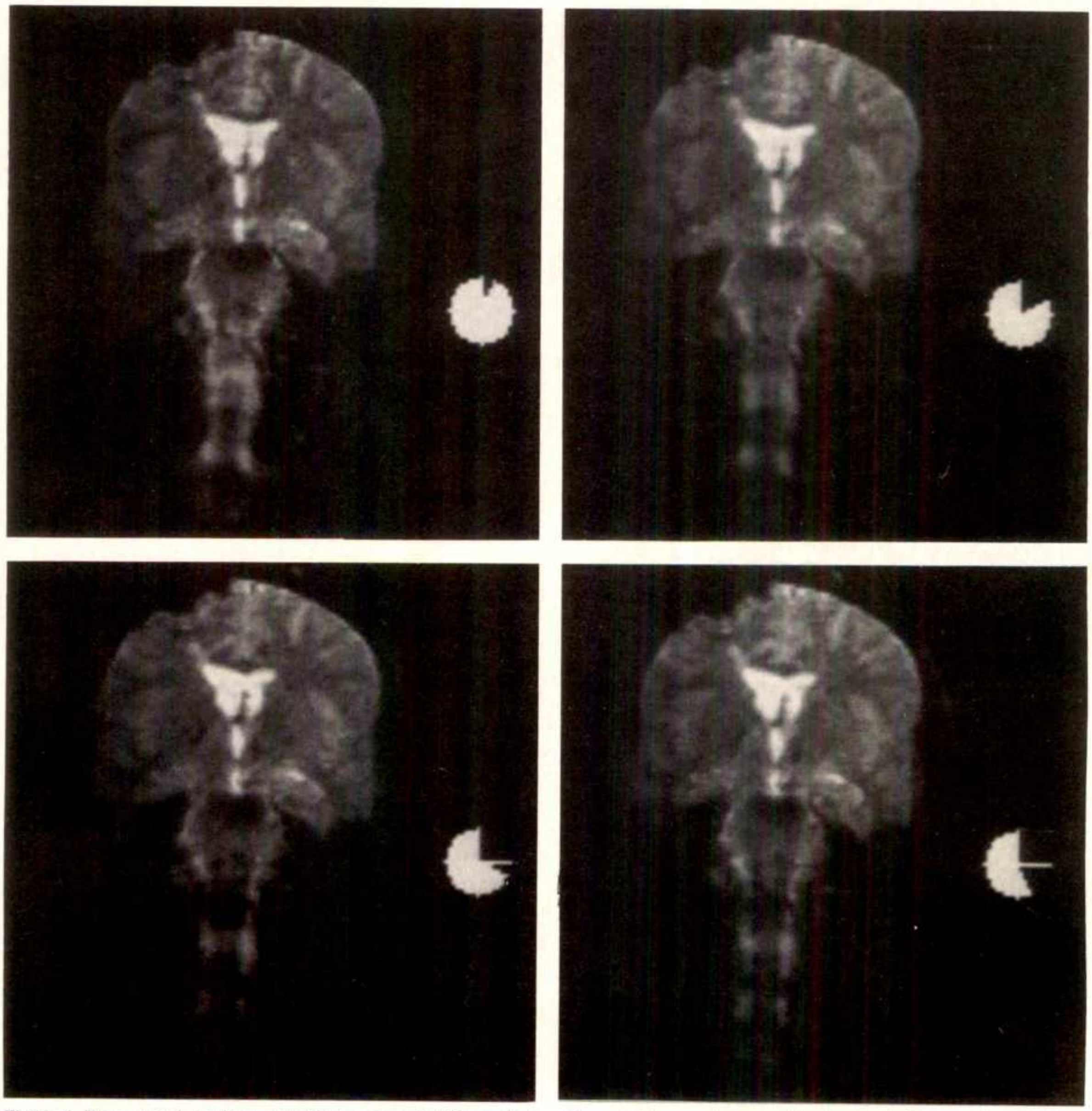

Figure 4. Four snapshots from a 16 frame coronal EPI movie loop through the cerebrum and brainstem is shown. Signal void in the subarachnoid spaces at the foramen magnum is caused by rapid CSF flow. Vascular pulsation related brain movement is more obvious when the sequence is displayed as a movie loop. (Ref. 04503.)

plane, that is along the bodies of the ventricles, whereas the latter represent in-plane rapid flow, which is assumed to be secondary to the jet of CSF ejected through the foramina of Monro in systole.

Eight frames from a transaxial 16 frame MBEST movie loop of the same patient are shown in Fig. 6 and again an area of signal attenuation is seen at the foramina of Monro during systole. As in the coronal movie loop, the flow pattern is more pronounced on the right side. These findings have been confirmed by preceding the MBEST sequence with a flow sensitizing sequence (Ordidge et al, 1989) in order to obtain quantifiable flow information. The flow sensitizing gradient was applied in the z-direction, *i.e.* along the patient axis. The z-component of CSF flow is mapped in Fig. 7 for three different phases of the cardiac cycle. Figures 7A, 7B and 7C correspond approximately to Figs 6C, 6G and 6H respectively. For uniform flow velocity v within a pixel, the image signal intensity, I, is given by $I \propto \sin kv$ where k is a constant determined by the flow encoding sequence parameters. The flow map demonstrates general low level flow throughout the ventricles (blue),

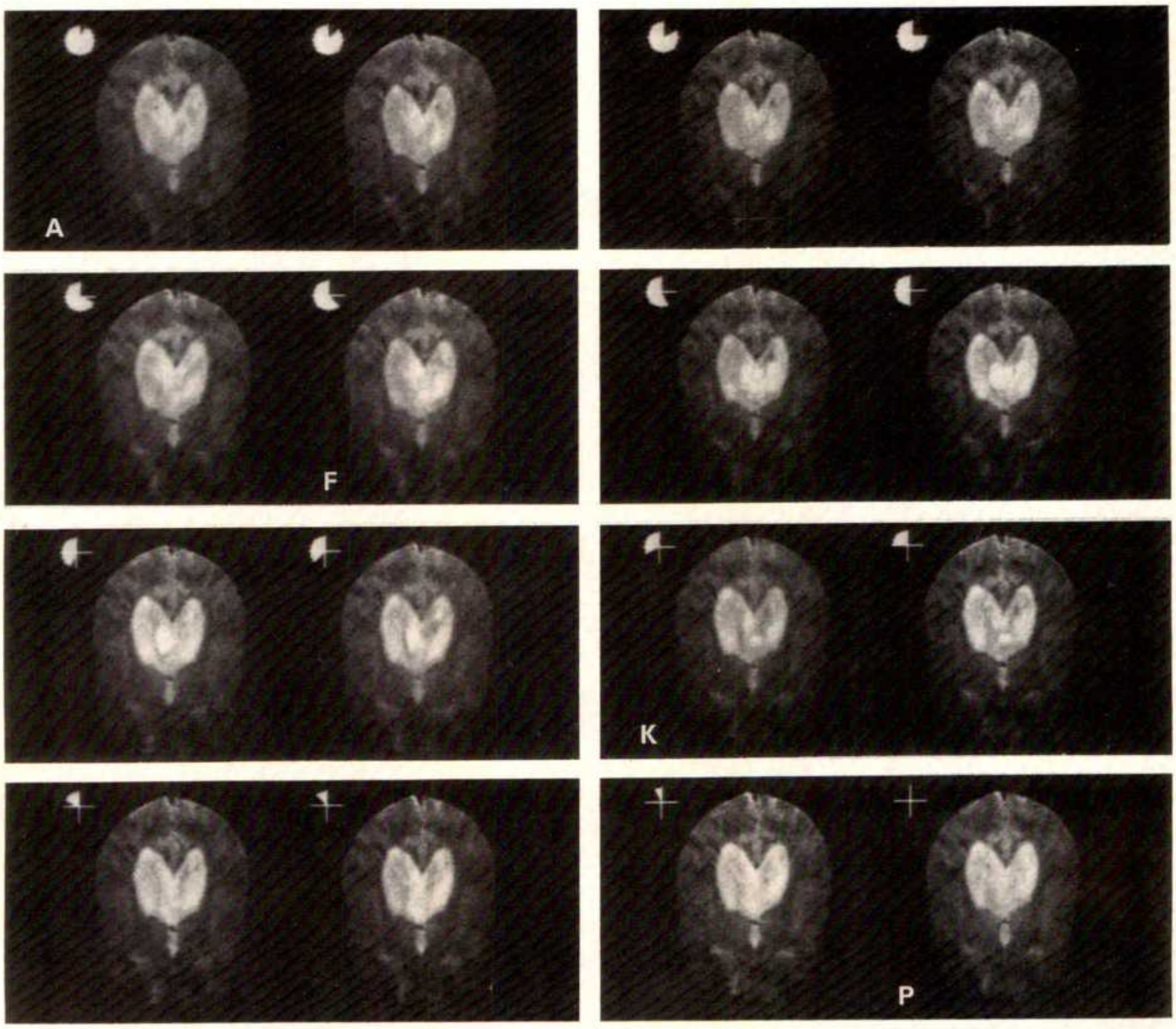

Figure 5. Sixteen frame coronal EPI movie loop through the lateral and third ventricle, posterior to the foramen of Monro. The clock indicates the phase of the cardiac cycle with respect to the R wave, frame A. Flow along the body of the ventricles appears bright owing to flow related enhancement. Dark areas reflect rapid flow, originating at the foramen of Monro. (Ref. 04004.)

and confirms the more rapid flow through the right foramen in systole (yellow and red). Note that the flow maximum is seen within the lateral ventricles. At the foramina, little signal is depicted, which may reflect turbulence resulting in loss of phase information.

Figure 8 shows six coronal 128 ms acquisition time EP images in a patient with communicating hydrocephalus. The imaging plane intersects the lateral ventricles, aqueduct and fourth ventricle. During systole (frames A–C), a flame shaped area of signal void due to flow can be seen to originate from the aqueduct and extend into the upper part of the fourth ventricle. This confirms that the aqueduct is patent. The flow plume decays away in frames D–F during diastole.

Figure 9 shows all 16 frames of a sagittal EPI movie loop in a patient with syringohydromyelia. Multiple areas of signal attenuation are seen in the fluid contained within the thin walls of the syrinx. These areas of signal loss indicate complex flow patterns within the fluid contained in the central cavity. Complex flow of CSF within syrinx cavities in five patients was also found by Le Bihan et al (1987), using the technique of mapping intravoxel incoherent motion.

Discussion

Approximately 500 ml of CSF are secreted each day, largely by the choroid plexus within each lateral ventricle, and this circulates through the ventricular system and the cerebral and spinal subarachnoid systems before being absorbed by the arachnoid villi which are associated with the major dural venous sinuses. Superimposed on the slow background of circulation of CSF are respiratory and cardiac depen-

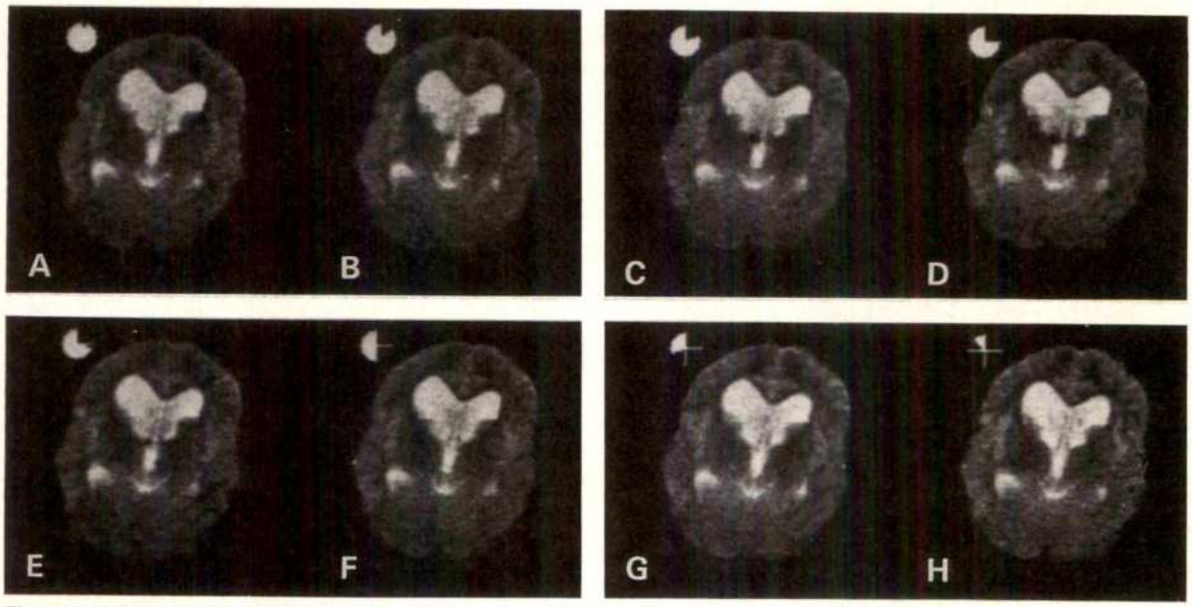

Figure 6. Eight transaxial MBEST images at the foramina of Monro of the same case as in Fig. 5. Signal enhancement due to flow is demonstrated at the foramina in systole (frames G and H). (Ref. 04005.)

dent pulsatile flows. The mechanisms of CSF propulsion along these pathways are still incompletely understood. Cardiac dependent CSF motion occurs secondarily to cerebral perfusion. The existence of a third ventricular pump has been postulated (O'Connell, 1943) and much support for this hypothesis has been provided through observations made during pneumoencephalography (Du Boulay et al, 1972). In a recent study in normal individuals using gated high resolution MRI (Mark et al, 1987), the flow results were best explained by postulating a synchronous pulsatile flow of CSF at the foramen of Monro and the aqueduct with an antegrade flow during systole and a retrograde but smaller flow during diastole, giving a net antegrade flow of CSF which enters the basal cisterns. The observation of pulsatile flow at the foramen of Monro suggests that the lateral ventricles do play a part in generating CSF flow, perhaps via expansion of the choroid plexus. Certainly considerable motion of CSF occurs within the lateral ventricles in pathological conditions, as we have observed in several cases in addition to the patient with aqueduct stenosis reported above.

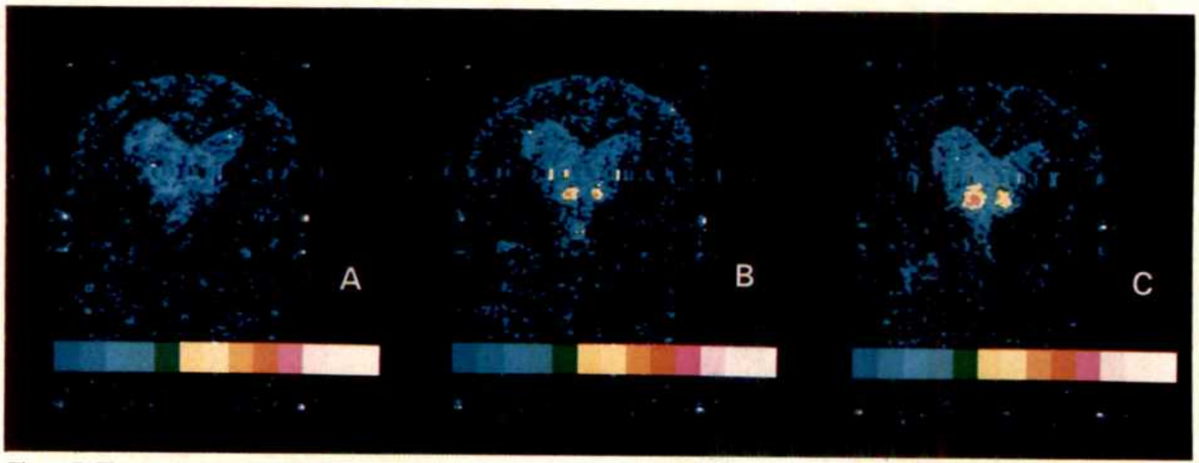

Figure 7. Flow maps obtained at different phases of the cardiac cycle in the same patient as Figs 5 and 6: (A) diastole; (B) early systole; (C) mid-systole. Flow sensitization is along the z-axis or patients axis, *i.e.* in a direction perpendicular to the plane of the flow maps. The flow velocity is proportional to arcsin(I), where I is the signal intensity in the map (blue, low intensity; white, high intensity). Flow is more pronounced in the right foramina of Monro, in accordance with the flow patterns in the standard MBEST images of Figs 5 and 6. (Ref. 04005.)

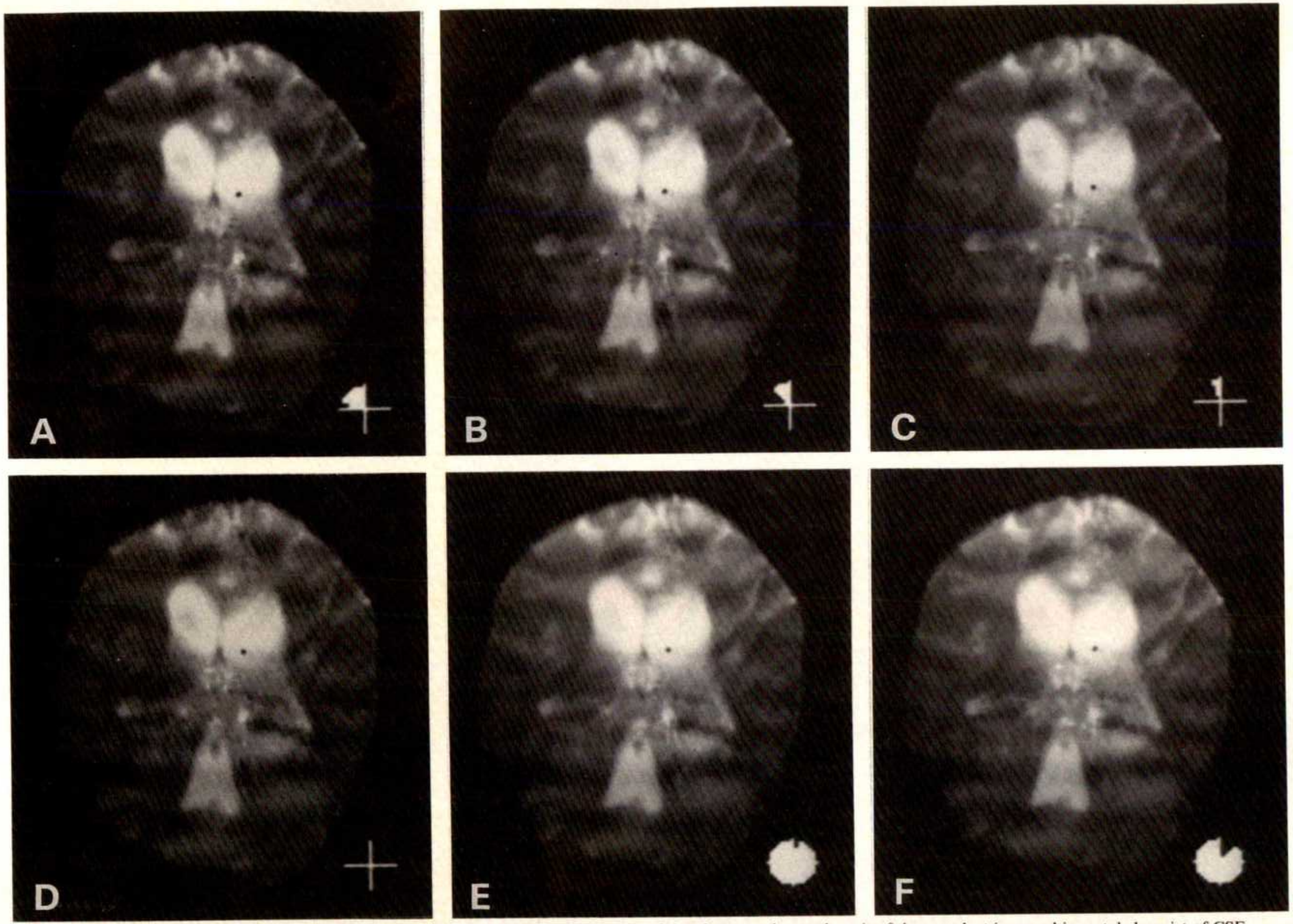

Figure 8. Six coronal EPI images showing the fourth ventricle. In Fig. 8 (A–C) the area of signal attenuation at the exit of the aqueduct is caused in systole by a jet of CSF projecting from the aqueduct into the fourth ventricle. The jet plume decays in diastole (D–F). (Ref. 21301.)

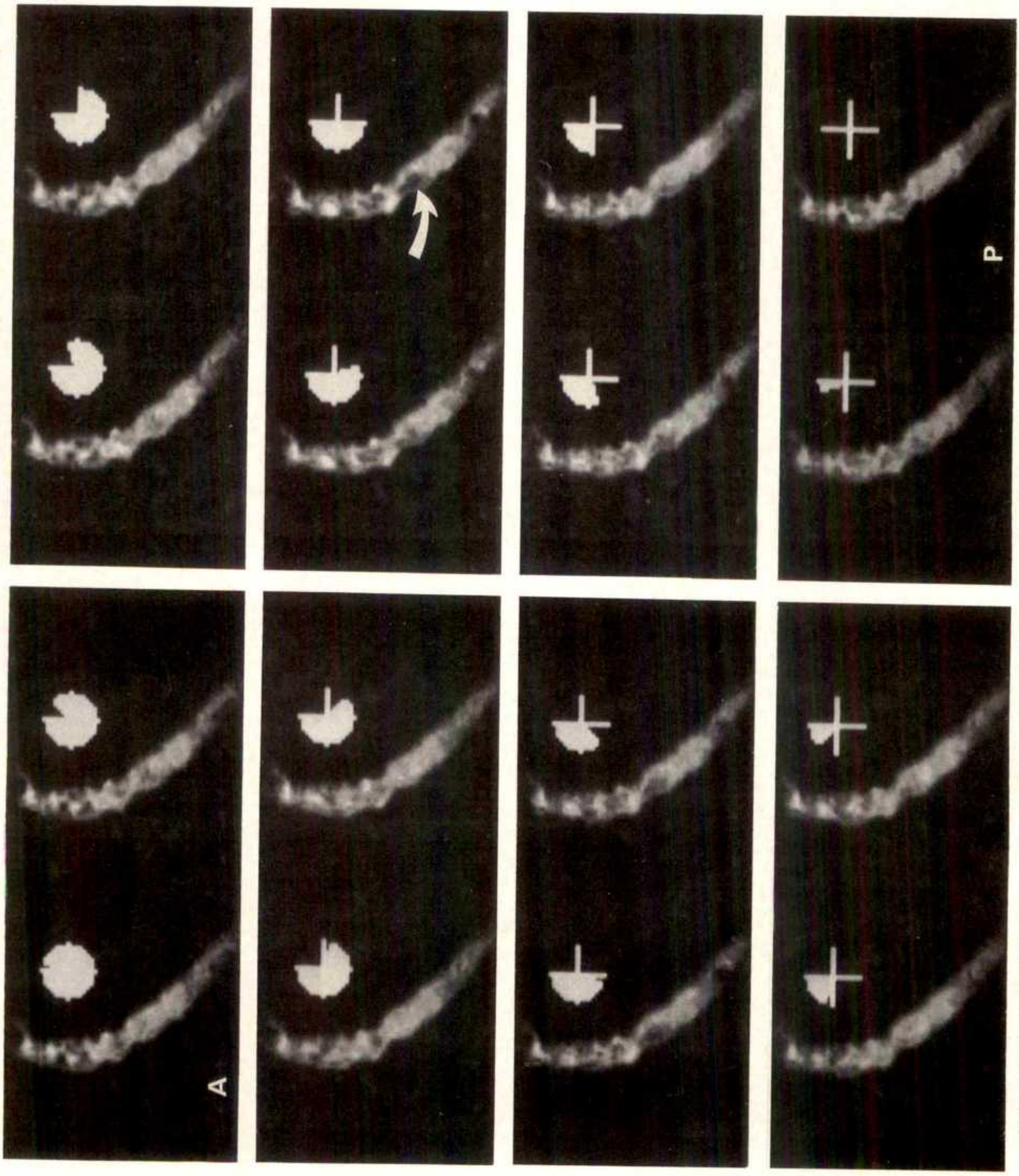

Figure 9. Sixteen frames of a sagittal EPI movie loop, showing intracavitary fluid flow in a syringohydromyelia. Areas of signal void indicate turbulent flow in eddies, which travel caudally during systole. Note the development of a jet in systole at the narrowed part of the spinal canal (arrow). (Ref. 21301.)

Conclusion

We have shown that EPI can be used to study flow patterns in the CSF pathways with high spatial and temporal resolution. In the MBEST technique, both real and imaginary components of the NMR signal are collected, from which magnitude and phase information can be derived and this can be used to study transient, complex CSF flow patterns in real time.

Using a flow encoding sequence (Ordidge et al, 1989), we have produced coronal maps indicating CSF flow in the lateral ventricles of a patient with aqueduct stenosis. In these results localized flow is a direct and quantifiable function of localized signal intensity. Our results indicate that EPI is able to provide both qualitative and quantitative information in real-time. This could be of value for studying CSF flow dynamics in both normal and abnormal situations.

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Fetal choroid plexus cysts: a prospective study and review of the literature

By P. Twining, FRCR, *J. Zuccollo, MBBS, J. Clewes, DMU and J. Swallow, DMU

Departments of Radiology and *Histopathology, Queen's Medical Centre, Nottingham, UK

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Abstract. To determine the incidence and significance of fetal choroid plexus cysts, a prospective study was carried out at Queen's Medical Centre, Nottingham. The incidence of cysts was found to be 0.42% and the size of cysts varied from 3 to 13 mm with a mean diameter of 6.2 mm. Choroid plexus cysts were associated with other fetal abnormalities in three cases, two of which were subsequently found to have a chromosomal abnormality, one Trisomy 18 and one Trisomy 21. A review of the reported cases of choroid plexus cysts reveals an overall incidence of 5.8% for Trisomy 18. We therefore recommend that in patients with choroid plexus cysts a detailed scan should be carried out to look for the ultrasound markers of Trisomy 18. If there is an associated abnormality or cysts are large (13 mm or greater in diameter) and bilateral then a karyotyping should be carried out.

The demonstration of fetal choroid plexus cysts has led to considerable debate about their clinical significance. Early reports (Bundy et al, 1986; Nicolaides et al, 1986; Furness, 1987; Ricketts et al, 1987) showed an association with Trisomy 18, whilst later larger series showed a normal outcome in fetuses with cysts (Clark et al, 1988; Deroo et al, 1988; Benacerraf & Laboda, 1989) (Table I).

We have conducted a prospective study and reviewed the literature.

Material and methods

At Queen's Medical Centre, Nottingham, routine booking scans are carried out at 18–20 weeks gestation. All scans are carried out at the ante-natal clinic using either a Hitachi 410, a Hitachi 450 or an IgE 3600 ultrasound machine. Detailed scans are carried out at the ante-natal clinic or in the X-ray department using an Acuson 128 scanner.

The routine booking scan includes a biparietal diameter measurement and an assessment of intracranial anatomy, in particular cerebellar and ventricular measurements. Choroid plexus cysts are defined as echo free areas within the highly reflective choroid which fills the posterior horn of the lateral ventricle (Fig. 1).

The size, position and number of the cysts are determined.

Patients with choroid plexus cysts are referred for a detailed scan 1 week after the initial booking scan and

Table I. Associated chromosomal abnormalities

Year	Reference	Number of cases	
1984	Chudleigh et al	5	Normal
1985	Friday et al	1	Normal
1986	Bundy et al	1	1 Trisomy 18
1986	Nicolaides et al	4	3 Trisomy 18
1987	Ricketts et al	4	1 Trisomy 21
1987	Ostlere et al	11	Normal
1987	Benacerraf	2	Normal
1987	Furness	30	3 Trisomy 18
1988	Chitkara et al	43	3 Trisomy 18
1988	Clark et al	5	Normal
1988	Deroo et al	17	Normal
1989	Benacerraf & Laboda	38	Normal
1989	Ostlere et al	42	2 Trisomy 18
1991	Twining et al[a]	19	1 Trisomy 18 1 Trisomy 21

[a] This work.

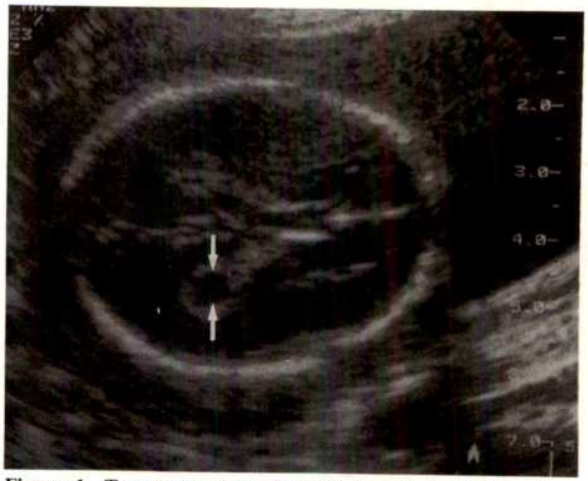

Figure 1. Transverse scan through lateral ventricles of an 18-week fetus showing a 5 mm choroid plexus cyst (indicated by arrows).

Table II. Incidence

Year	Reference	Incidence	Number of cases
1991	Twining et al[a]	0.42%	19
1988	Clark et al	0.18%	5
1988	Deroo et al	0.8%	17
1988	Chitkara et al	0.65%	41
1987	Furness et al	0.7%	30
1987	Ostlere et al	0.34%	11

[a] This work.

are also re-scanned at 22 weeks to assess resolution of the cysts.

Results

Over an 11-month period 4541 singleton pregnancies were scanned and 19 fetuses were identified with choroid plexus cysts, an incidence of 0.42%. Incidences quoted in other series range from 0.18 to 0.8% (Table II). Cysts were unilateral in 10 cases and bilateral in nine cases. The diameter of the cysts varied from 3 to 13 mm with a mean diameter of 6.2 mm.

Three fetuses demonstrated an associated abnormality. The first showed a diaphragmatic hernia and bilateral radial aplasia. The patient opted for termination of pregnancy; chromosomal studies revealed Trisomy 18. A second fetus initially scanned at 18 weeks showed large bilateral choroid plexus cysts (measuring 10 mm and 13 mm), the largest in our series (Fig. 2). The patient was re-scanned at 22 weeks at which time the cysts were resolving. The fetus, however, had developed the "double bubble" appearance typical of duodenal atresia. The patient declined amniocentesis and delivered a live baby at term. Subsequent chromosomal studies revealed Trisomy 21. The third fetus had a small omphalocoele and amniocentesis showed a normal karyotype.

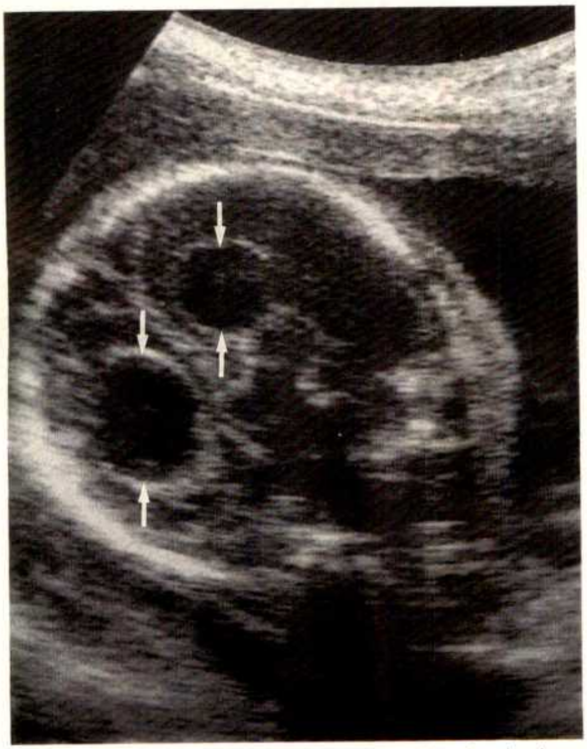

Figure 2. Coronal scan through lateral ventricles showing large bilateral choroid plexus cysts (indicated by arrows).

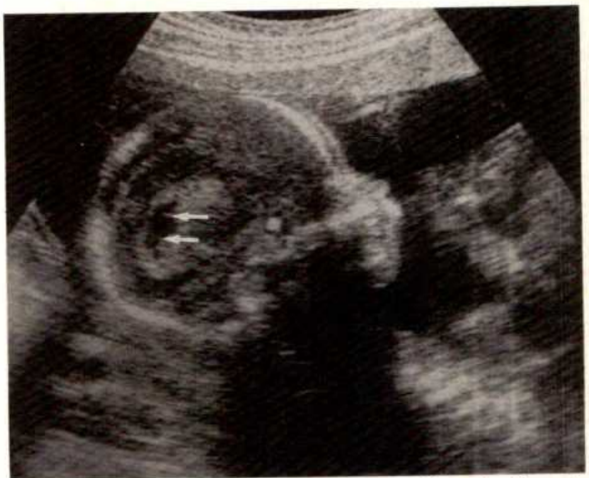

Figure 3. Sagittal scan through lateral ventricles of a 22-week fetus showing fine septa within a choroid plexus cyst (arrows show septa).

All choroid plexus cysts seen at 18 weeks had either resolved or were considerably smaller when re-scanned at 22 weeks. In a number of cases unilocular cysts became smaller and demonstrated fine septa at 22 weeks (Fig. 3) before disappearing at 24 weeks, and this may be part of the natural history of their resolution.

Discussion

A review of the literature including our own series reveals 222 cases of choroid plexus cysts associated with 13 cases of Trisomy 18 and two cases of Trisomy 21 (Chudleigh et al, 1984; Friday et al, 1985; Benacerraf, 1987; Ostlere et al, 1987; Chitkara et al, 1988; Ostlere et al, 1989): an overall incidence of 5.8% for Trisomy 18

Table III. The relationship of the size of choroid plexus cysts and Trisomy abnormalities

Year	Reference		
1986	Bundy et al	Large bilateral cysts	Trisomy 18
1987	Furness et al	Large bilateral cysts	Trisomy 18
1988	Chitkara et al	Bilateral 20 mm cysts	Trisomy 18
1991	Twining et al[a]	Bilateral 13/10 mm cysts	Trisomy 21

[a] This work.

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Table IV. Fetal abnormalities in Trisomy 18 (six cases)

		Number of cases
Hands	Fixed flexion deformities with overlapping fingers	5
	Radial aplasia	1
Feet	Rockerbottom feet	1
	Prominent heels	2
	Syndactyly	1
Face	Micrognathia	2
	Cleft lip	1
Thorax	Diaphragmatic hernia	2
Congenital heart disease	Ventricular septal defect	5
	Single ventricle	1
	Overriding aorta	1
Abdomen	Horseshoe kidney	2
	Unilateral hydronephrosis	1
Intrauterine growth retardation		6
Polyhydramnios		2

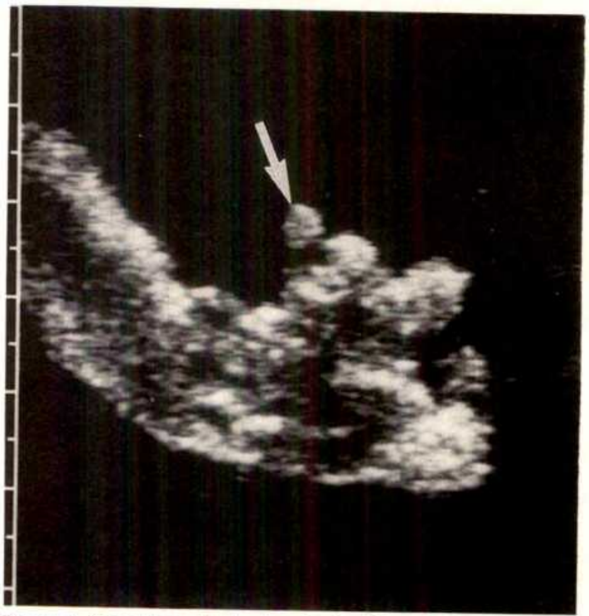

Figure 5. Scan through the hand of a 28-week fetus showing overlapping of the fingers with flexion deformities (arrow points to fifth finger overlapping fourth).

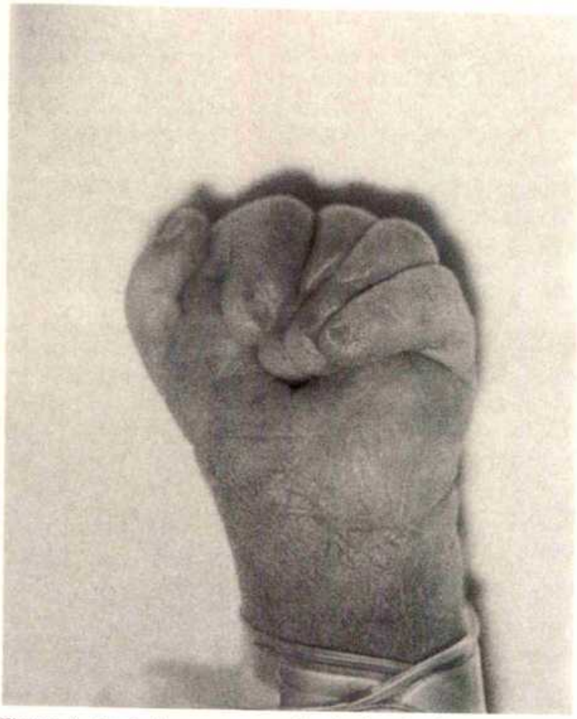

Figure 4. Typical appearances in the hand of a term fetus showing (overlapping) flexion deformities of the fingers.

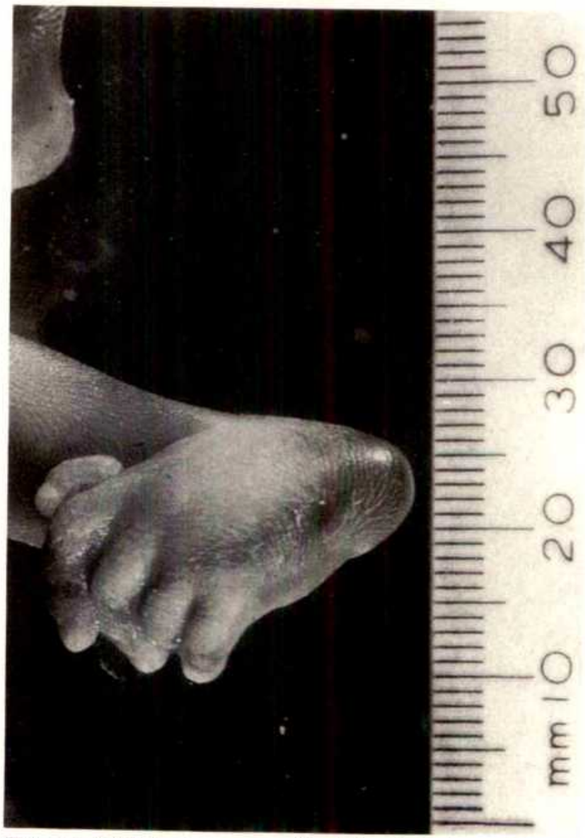

Figure 6. Typical appearance of radial aplasia in an 18-week fetus.

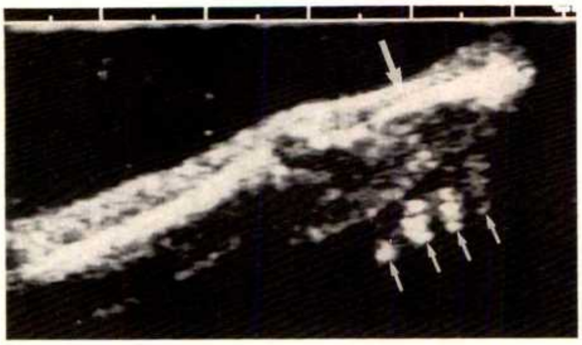

Figure 7. Scan of fetus in Fig. 6 showing the characteristic ultrasound appearance of radial aplasia (large arrow points to ulna, small arrows to fingers).

and 0.9% for Trisomy 21. A recent study of 14 cases of Trisomy 18 (Fitzsimmons et al, 1989) showed choroid plexus cysts present in 70% of fetuses under 26 weeks gestation. There appears therefore to be a definite association between choroid plexus cysts and Trisomy abnormalities, particularly Trisomy 18.

The size of the cysts is also important as four of these chromosomally abnormal fetuses (three Trisomy 18 and one Trisomy 21) were associated with large bilateral cysts (Table III).

Over the past 2 years we have seen six cases of Trisomy 18 and all six cases demonstrated characteristic abnormalities of either the extremities, face or internal organs (Table IV). The most typical abnormalities in the extremities are fixed flexion deformities in the hands with overlapping of the fifth finger over the fourth finger, and index over the third finger (Figs 4 and 5). Radial aplasia was also seen (Figs 6 and 7) with "rockerbottom feet", syndactyly and prominence of the heels (Fig. 8) in the lower limb. Micrognathia (Fig. 9) and cleft lip are characteristic findings as are cardiac abnormalities and diaphragmatic herniae. All fetuses showed growth retardation and two demonstrated polyhydramnios.

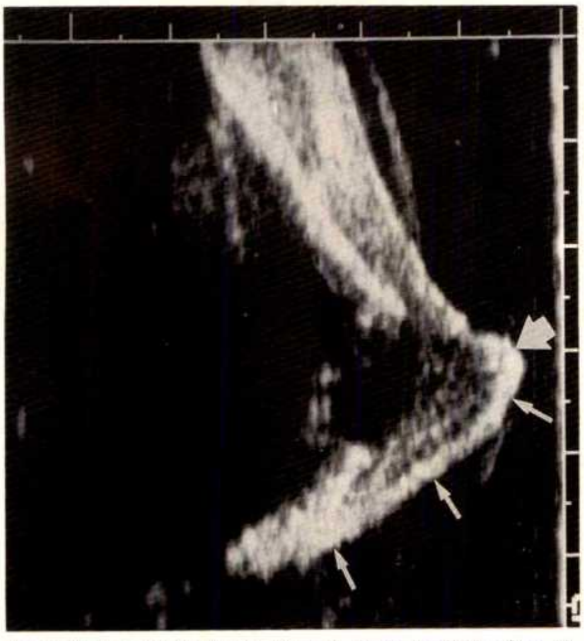

Figure 8. Longitudinal scan through the lower limb of an 18-week fetus showing prominence of the heel (large arrow), and rockerbottom foot (small arrows).

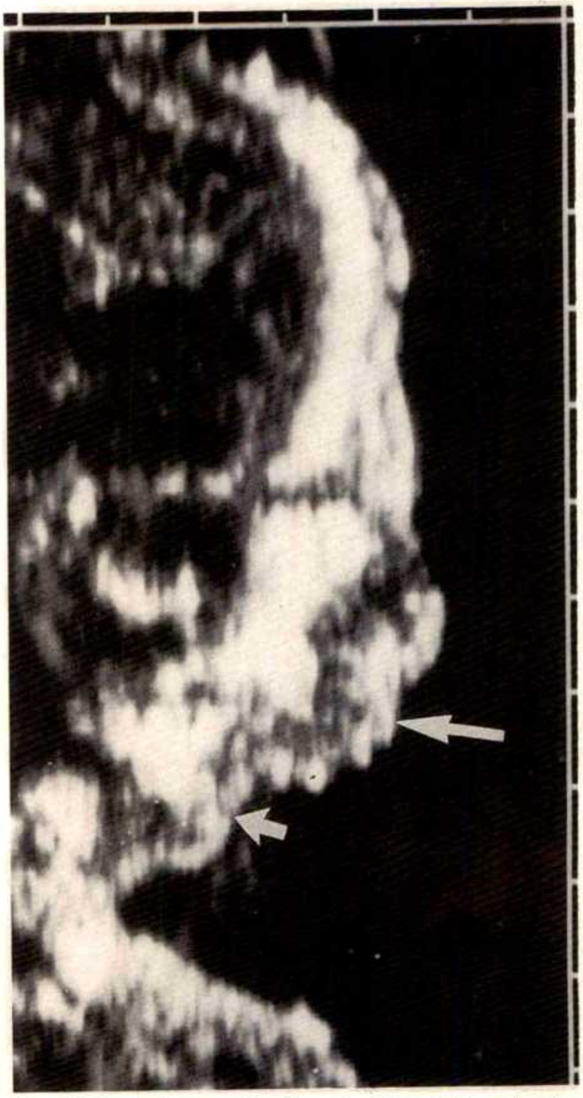

Figure 9. Sagittal scan of the face of a 20-week fetus showing micrognathia. (Large arrow points to normal upper mandible; smaller arrow to hypoplastic lower mandible.)

We recommend that all patients with choroid plexus cysts have a detailed scan to look for ultrasound markers of Trisomy 18. Particular attention should be paid to the hands, feet, face and thorax. When any other abnormality is found, or if cysts are large (13 mm or greater in diameter) and bilateral, karyotyping should be performed.

Acknowledgments

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The chest radiograph appearances seen following high dose chemotherapy and autologous bone marrow transplantation for resistant malignant lymphoma

By *F. C. Millard, MA, FRCS, *R. A. Nakielny, MA, FRCR, †M. Makris, BA, MRCP and †D. A. Winfield, FRCP, FRCPath

Departments of *Radiology and †Haematology, Royal Hallamshire Hospital, Sheffield, UK

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Keywords: Chest radiograph, Chemotherapy, Autologous bone marrow transplantation, Malignant lymphoma

Abstract. The objective of this study was to review and analyse the chest radiograph (CXR) appearances seen following high dose chemotherapy and autologous bone marrow transplantation (ABMT), and to identify any characteristic patterns. Thirty-one patients underwent ABMT between 1984 and 1989 for high grade lymphoma resistant to conventional chemotherapy. Their case notes and CXRs were reviewed in conjunction with the clinicians. In this small sample of patients, an acute interstitial pattern was seen with pulmonary oedema following bone marrow reinfusion in two cases of the 13 patients showing CXR changes (15%). Otherwise, the CXR changes following ABMT were not specific, although they did alert the clinician to the possibilities of recurrent lymphoma or opportunistic infection, enabling appropriate investigations and treatment to be instituted at an early stage. The complications and CXR changes did not differ greatly from those seen following allogeneic bone marrow transplantation.

Lymphoma patients who fail to achieve complete remission after conventional chemotherapy have a poor prognosis. Lymphomas have a steep dose–response curve for cytotoxic chemotherapy but dose escalation is limited by myelosuppression. By harvesting and storing bone marrow which is not involved with disease outside the body while high dose chemotherapy is given, this problem may be overcome (Herzig, 1981).

Two major problems associated with the procedure are infections during the pancytopenic phase following the chemotherapy and lymphoma recurrence. While the chest radiograph (CXR) appearances following allogeneic bone marrow transplantation have been reviewed (Wise et al, 1984; Branson & Durham, 1986; Link et al, 1986) those following autologous bone marrow transplantation (ABMT) have not been previously described.

Here we describe our radiological experience of CXR appearances following ABMT and discuss possible characteristic patterns.

Subjects and methods

The CXRs and clinical records of our first 31 patients who underwent ABMT following failure of conventional chemotheraphy were reviewed retrospectively. Chest radiographs were taken prior to ABMT as a baseline, and thereafter at weekly intervals or more frequently during periods of pulmonary disease.

Patient characteristics are shown in Table I. All the non-Hodgkin's lymphomas were high grade (Kiel classification). The histology of the Hodgkin's lymphoma patients was as follows: nodular sclerosing 12 (71%), mixed cellularity four (24%) and lymphocyte depleted one (5%).

Bilateral bone marrow trephines were performed on all patients and only those with bone marrow free of disease were considered suitable.

Bone marrow (750–1000 ml) was harvested from posterior and anterior iliac crests and sternum under general anaesthesia. The nucleated cells in the marrow were separated using dextran sedimentation and suspended in dimethyl sulphoxide and fresh frozen plasma to a final volume of 480 ml. This was stored in liquid nitrogen until its return to the patient 24 h after the last dose of chemotherapy. The frozen bone marrow was defrosted at the patient's bedside in a 37°C waterbath and given intravenously in a fast running infusion. The marrow contained some free haemoglobin from damaged red cells and to prevent renal impairment, patients were given 4 l of normal saline intravenously over 24 h following the marrow return to ensure an

Table I. Patient characteristics

	Hodgkin's	Non-Hodgkin's
Number	17	14
Age (years)		
mean	31.6	37.3
range	17–51	15–57
Sex (% male)	67	64
Diagnosis to ABMT (months)		
mean	35	11
range	11–96	5–29

Address correspondence to Dr F. C. Millard, X-Ray Department, C Floor, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF.

Table II. Chemotherapy

	Day						
	1	2	3	4	5	6	7
BCNU 300 mg/m²	*						
Etoposide 200 mg/m² IV		*	*	*	*		
Cytosine 100 mg/m² IV BD		**	**	**	**		
Melphalan 140 mg/m² IV						*	
Bone marrow reinfusion							*

*One dose.

adequate diuresis. The mean number of bone marrow nucleated cells returned to the patient was 3.02×18^8/kg (range $(1.21\text{–}6.4) \times 10^8$/kg). The chemotherapy regime is shown in Table II. The first 13 patients received cyclophosphamide (1.5 g/m² intravenously on Days 1–4) instead of melphalan. The patients receiving cyclophosphamide received etoposide at the reduced dose of 75 mg/m².

No radiotherapy was used in the induction phase. All patients had Hickman lines and were nursed in side rooms without barrier nursing.

Results

In 18 of the 31 patients, no change in the CXR occurred following ABMT. In the 13 remaining patients these changes were classified into the following patterns: acute and subacute alveolar, and acute and subacute interstitial (Table III). A period of 72 h was used to distinguish acute from subacute. Changes after 28 days were classified as chronic.

The meaning of interstitial will be specified for each case. When mixed patterns were seen the most prominent was chosen. An acute interstitial pattern (Kerley B lines) was seen in two patients (15%) as a result of pulmonary oedema associated with bone marrow reinfusion. This responded to diuretic therapy.

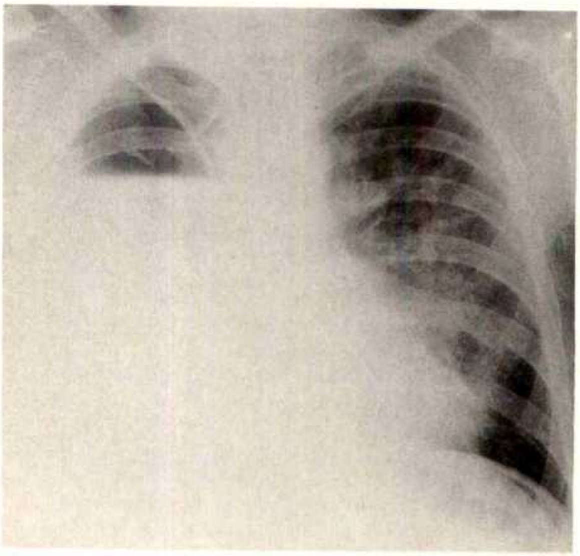

Figure 1. Chest radiograph showing subacute reticulonodular (2–5 mm) with added alveolar patterns, as a result of recurrent lymphoma, diagnosed at post mortem. This patient had had a right pneumonectomy for Hodgkin's lymphoma prior to ABMT (Case 3).

Two patients (15%) developed a subacute interstitial pattern–reticulonodular (2–5 mm). One of these two cases was seen in conjunction with an alveolar pattern and both were associated with recurrent lymphoma (Figs 1 and 2). Subacute alveolar shadowing was seen in nine patients (69%). Three were due to recurrent lymphoma, two of these being associated with cavitation (Fig. 3). The site of recurrence was remote from previous lesions. A further four cases were secondary to pneumonia. It was not possible to distinguish chest infection from recurrent disease on clinical grounds. The

Table III. Chest radiograph appearances following ABMT

Case number	Radiological features of CXR and their time of onset	Diagnosis	Diagnostic method
1	Acute interstitial within 24 h	Pulmonary oedema	Clinical
2	Acute interstitial within 24 h	Pulmonary oedema	Clinical
3	Subacute interstitial (and alveolar) 21 days	Recurrent lymphoma	Post-mortem
4	Subacute interstitial 28 days	Recurrent lymphoma	Open lung biopsy
5	Subacute alveolar (and cavitation) 12 days	Recurrent lymphoma	Clinical[a]
6	Subacute alveolar 6 days	Recurrent lymphoma	Post-mortem
7	Subacute alveolar (and cavitation) 21 days	Recurrent lymphoma	Open lung biopsy
8	Subacute alveolar 28 days	Bacterial pneumonia	Post-mortem
9	Subacute alveolar 12 days	Tuberculous pneumonia	Sputum culture
10	Subacute alveolar 14 days	Broncho-pulmonary aspergillosis	Post-mortem
11	Chronic alveolar 5 months	Non-specific pneumonia	Clinical[b]
12	Subacute alveolar 21 days	Unknown	—
13	Subacute alveolar 14 days	Unknown	—

[a] Permission for post-mortem was withheld.

[b] This patient remained well during this time and further investigation was felt unwarranted. The changes resolved spontaneously.

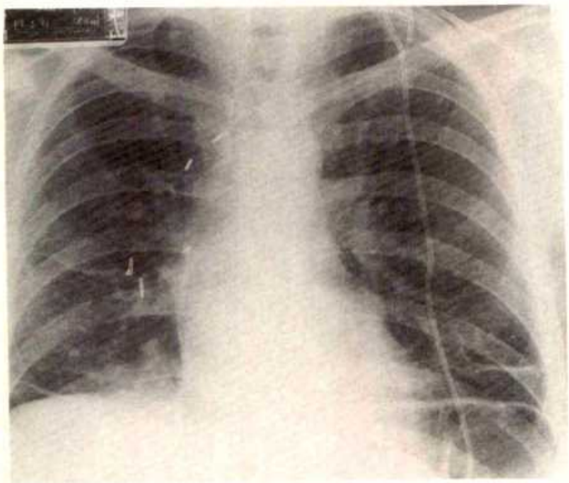

Figure 2. Chest radiograph showing a subacute reticulonodular (2–5 mm) pattern as a result of recurrent non-Hodgkin's lymphoma, diagnosed at open lung biopsy. The patient had had previous thymectomy at presentation with lymphoma (Case 4).

patient with tuberculous pneumonia (Fig. 4) also developed a tuberculous extradural abscess within the cervical spine. He died from these complications 2 months following ABMT. Broncho-pulmonary aspergillosis occurred in one case when an alveolar pattern was seen at both lung bases (Fig. 5). In two cases the cause was not established.

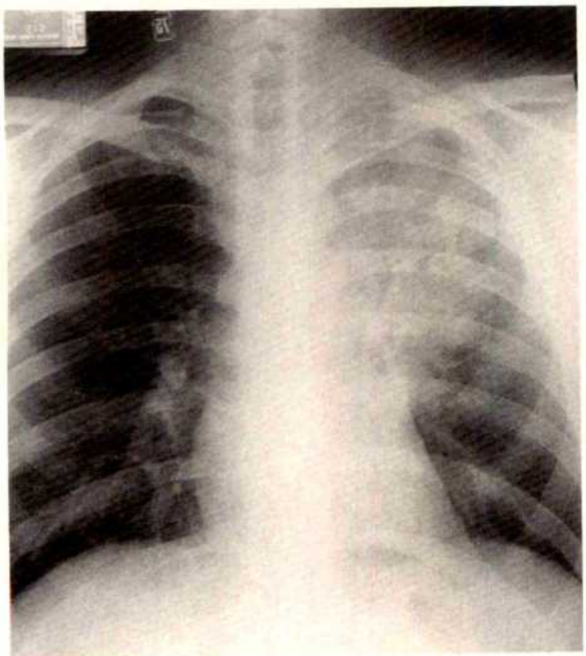

Figure 3. Chest radiograph showing an alveolar pattern in the left upper lobe with cavitation, as a result of recurrent Hodgkin's lymphoma, diagnosed at open lung biopsy (Case 7).

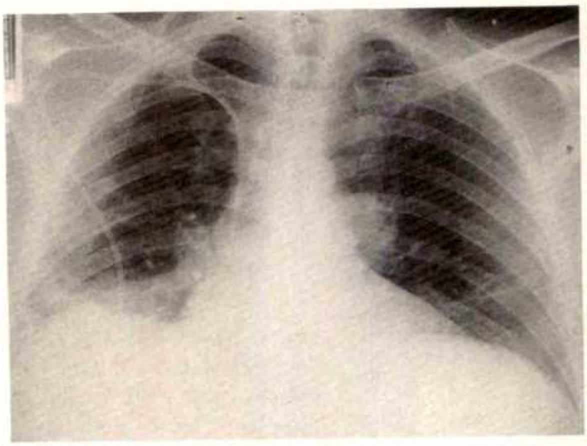

Figure 4. Chest radiograph showing an alveolar pattern as a result of tuberculosis diagnosed on sputum culture (Case 9).

Discussion

Following high dose chemotherapy and ABMT, the pulmonary complications of pneumonia and lymphoma relapse are a major cause of morbidity and mortality. It would be most helpful therefore, if an early diagnosis could be made by analysis of CXR appearance. While this problem has been examined in allogeneic bone marrow transplantation (Wise et al, 1984; Branson & Durham, 1986; Link et al, 1986), it has not yet been addressed in ABMT.

In this study, an acute interstitial pattern was associated with pulmonary oedema following marrow reinfusion in two patients (15%). Possible causes include the

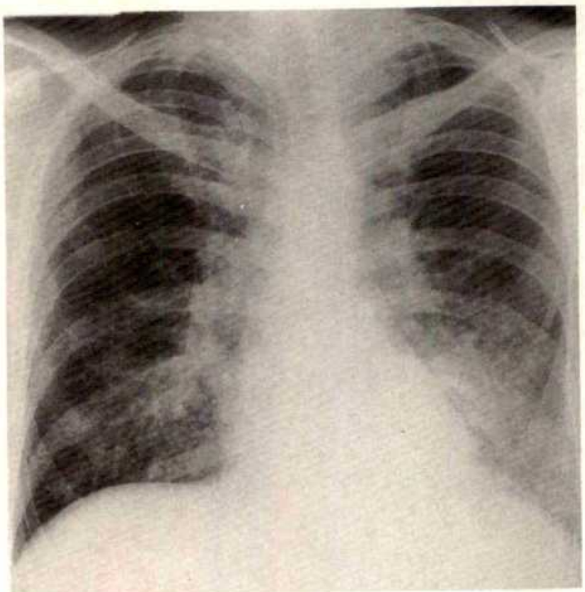

Figure 5. Chest radiograph showing an alveolar pattern at both lung bases as a result of bronchopulmonary aspergillosis diagnosed at post mortem (Case 10).

high fluid load given following the bone marrow reinfusion in an attempt to prevent renal damage from the free haemoglobin in the marrow, or a reaction to the cryoprotective agent DMSO, in which the marrow is kept.

A subacute interstitial pattern was seen with recurrent lymphoma (15%); in one of these two patients, alveolar changes were also seen superimposed on the predominantly subacute interstitial pattern. No patient developed progressive interstitial pneumonia following ABMT. This complication has been reported in some 25% of allogeneic bone marrow transplant patients, when cytomegalovirus (CMV) was the common causative pathogen accounting for 30–70% of cases (Olliff & Williams, 1989; Wise et al, 1984). The reason for the absence of CMV pneumonitis in this series could be the use of CMV negative blood products in CMV negative patients, the lack of pre-transplant radiation injury to the lungs from total body irradiation, or the absence of graft versus host disease. Subacute alveolar changes were seen with recurrent lymphoma (23%), as well as with pneumonias (31%). It is important to stress that both tuberculous and fungal infections should be considered as a potential cause of pneumonia in these immunocompromised patients. As in allogeneic marrow transplantation (Kurzock et al, 1984) diagnosis can be difficult owing to atypical presentation, initial negative culture results, and the presence of more than one pathogen. Although no examples were seen in our series, bacterial pneumonia may produce little or no CXR changes during the neutropenic phase and pneumonic infiltrates may only appear as the patients' own granulocyte production begins (Link et al, 1986).

In this small sample, no features on CXR (pattern, distribution or associated features) distinguishing pneumonia from lymphoma were identified.

Conclusions are necessarily difficult to draw with the small numbers of patients treated by AMBT. In this series, an acute interstitial pattern, developing shortly after marrow reinfusion, was associated with pulmonary oedema. Otherwise, analysis of CXR appearances following ABMT was not able to establish a specific diagnosis, although the prompt detection of changes does alert the clinicians to initiate investigation and appropriate treatment at an early stage. That a pneumonia may produce little or no CXR changes in a neutropenic patient should always be considered. With the exception of graft versus host disease and radiation pneumonitis, the complications and CXR changes following ABMT did not differ greatly from those seen following allogeneic bone marrow transplantation.

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Sonographic detection of foreign bodies of the extremities

By B. Banerjee, FRCS, FRCR and *R. K. Das, FRCS

Radiology and *Accident and Emergency Departments, Tameside General Hospital, Fountain Street,
Ashton-under-Lyne, Lancashire OL6 9RW, UK

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Keywords: Ultrasound, Radio-opaque foreign bodies, Radio-lucent foreign bodies, Detection, Localization

Abstract. A propspective study to assess the accuracy of ultrasound in the detection and localization of foreign bodies of the extremities was undertaken. Forty-five patients with clinical suspicion of foreign bodies were included in the study. Among 20 patients with radio-opaque foreign bodies, ultrasonic detection of foreign bodies was achieved in 19 patients. In 25 patients, with no radiographic evidence of foreign body, ultrasonic detection of foreign bodies was made in seven patients and among these foreign bodies were confirmed and removed at surgery in five patients. Accurate pre-operative ultrasonic localization of foreign bodies was carried out in three patients.

Every year, a large number of patients attend accident and emergency departments with suspected foreign bodies in the soft tissue of the extremities. Conventionally, plain radiography is used for confirmation, and for localization during surgery fluoroscopy is performed. Owing to improvement of image quality, sonography has recently gained wide acceptance in the evaluation of muscle, tendons and superficial soft tissue (Fornage et al, 1983). New high resolution ultrasonic machines with high frequency transducers can image objects as small as 0.5 mm to 1 mm, at depths varying from 4 cm to the skin surface (Walter, 1985). Ultrasonic imaging, therefore, can be gainfully employed to detect and to localize foreign bodies of the extremities. The aims of this study were to evaluate the accuracy of ultrasound in the detection of radio-opaque and radio-lucent foreign bodies and also in the pre-operative localization of the foreign bodies.

Methods and materials

Forty-five patients included in the study attended the Accident and Emergency Department at Tameside General Hospital with suspected soft tissue foreign bodies in the extremities. Following initial examination and routine radiography of the extremity for foreign bodies, the patients were independently selected for the study by a senior casualty physician. The patients were then referred to the sonologist for ultrasonic examination for foreign bodies. The sonologist had no prior knowledge of the radiographic findings and therefore ultrasonic examinations were not prejudiced or influenced by any plain radiographic findings. Sonography was performed with Toshiba SAL-77A and Siemens SL-2; 5 MHz and 7.5 MHz probes were used. A commercially available stand-off gel material was used for good contact between skin and probe. Gel blocks cut to different thicknesses and shapes were used for optimal delineation of the skin surface and superficial tissue. In three patients the foreign bodies were deep seated and required localization prior to or during surgery. This was carried out sonographically in lieu of conventional per-operative fluoroscopy. For sonographic localization of the foreign body, the suspected area was scanned in both longitudinal and horizontal planes. When the foreign body was located, a mark was placed on the skin directly over it. Care was taken to mark the skin nearest to the foreign body and on a proposed line of incision for the exploration. Its depth from the skin was measured using electronic callipers and noted in the report (Fig. 1).

Results

Among 45 patients in the study, routine radiographs demonstrated radio-opaque foreign bodies in 20 patients. In this group of patients, ultrasound detected foreign bodies in 19. In one patient, ultrasound failed to detect the radio-opaque foreign body. The cause of this failure was thought to be the presence of gas in the soft tissue underlying the foreign body. In 17 patients exploration for foreign bodies was carried out, and foreign bodies were found and removed in all cases. In the remaining 25 patients, although there was strong clinical suspicion of a foreign body, none was found on routine radiographs. Among these, ultrasound detected foreign bodies in seven patients. Eight patients underwent surgical exploration, including all seven patients with positive sonography and one patient with negative sonography but strong clinical suspicion of foreign body.

Exploration for foreign bodies was positive in five patients. Glass particles were removed from three patients, and a wooden splinter and a thorn were removed from the remaining two patients. Among three

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Address correspondence to Dr B. Banerjee, Consultant Radiologist, Tameside General Hospital, Ashton-under-Lyne, Lancashire.

Table I. Detection of foreign bodies
Total number of cases, 45
Suspected cases of foreign body with positive radiograph, 20 (Group A)
Suspected cases of foreign body with negative radiograph, 25 (Group B)

	Group A	Group B
Foreign bodies detected	19	7
Number of cases for exploration	17	8 (7 positive ultrasound, 1 negative ultrasound)
Positive exploration	17	5 (3 glass, 2 wooden splinter)
Negative exploration	Nil	3 (2 positive ultrasound, 1 negative ultrasound)

patients with a negative exploration, foreign bodies were suspected by ultrasound in two. In one patient, although no definite foreign body was found, only calcific material was removed at surgery, and in the other no foreign body was detected. The results are summarized in Table I. Pre-operative localization was carried out in three patients and all these localizations were found to be accurate at subsequent exploration.

Discussion

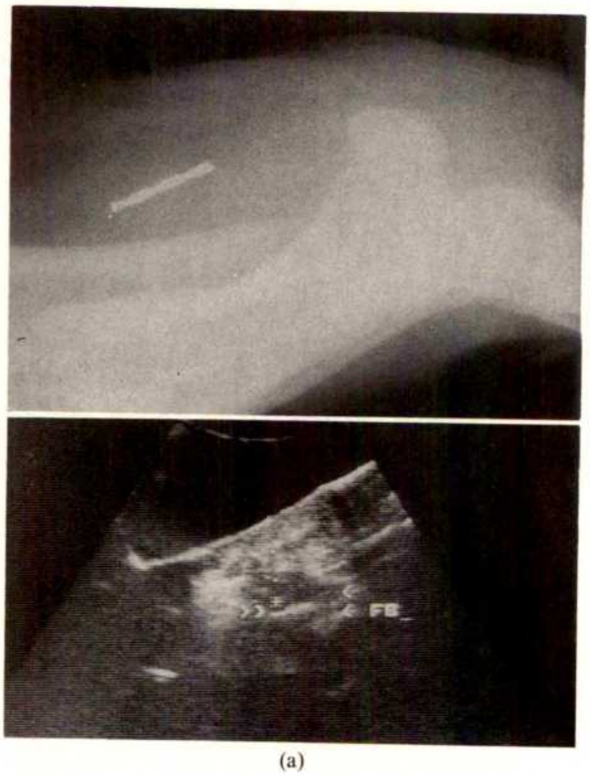
Metallic foreign bodies are readily detected radiographically but the radio-opacity of glass depends on the thickness of the fragment and on its lead content. The radio-opacity of glass thus ranges from moderately radio-opaque to almost radiolucent and therefore some glass particles embedded in soft tissue may not be detected by radiography. Wood and vegetable fragments are normally radiolucent.

Sonographic features of foreign bodies in the soft tissue have three components. Firstly, the appearance of the foreign bodies; secondly, the changes in the soft tissue surrounding the foreign bodies; thirdly, the appearance of soft tissue distal to the foreign bodies.

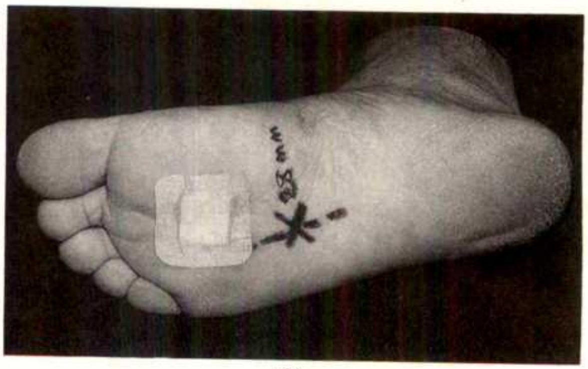
On sonography, all foreign bodies, whether radio-opaque or radiolucent are displayed as hyperechoic foci. The reflectivity depends on the acoustic impedance of the foreign body which, in turn, varies with the density of the particles. The sound reflects from the anterior surface of the foreign body, resulting in an echo-rich focus, but owing to poor penetration through the substance of the foreign body, its outline is rarely displayed. Ultrasound is therefore a poor indicator of the size and shape of the foreign bodies, which are better demonstrated by conventional radiography (Fig. 2).

The changes surrounding the foreign bodies are due to inflammatory reaction which may range from tissue oedema to abscess formation.

The inflammatory process requires some time to establish, hence this change may not be seen following recent trauma. Ultrasonically, the inflammatory tissue reaction is demonstrated as a hypoechoic rim surrounding the echogenic foreign body. This can be a



(a)



(b)

Figure 1. (a) Plain radiograph and ultrasound scan demonstrating a metallic foreign body in the sole of the foot. The depth of the foreign body under the skin surface was measured and recorded by electronic calipers. (b) The skin is marked directly over the foreign body on the proposed line of incision.

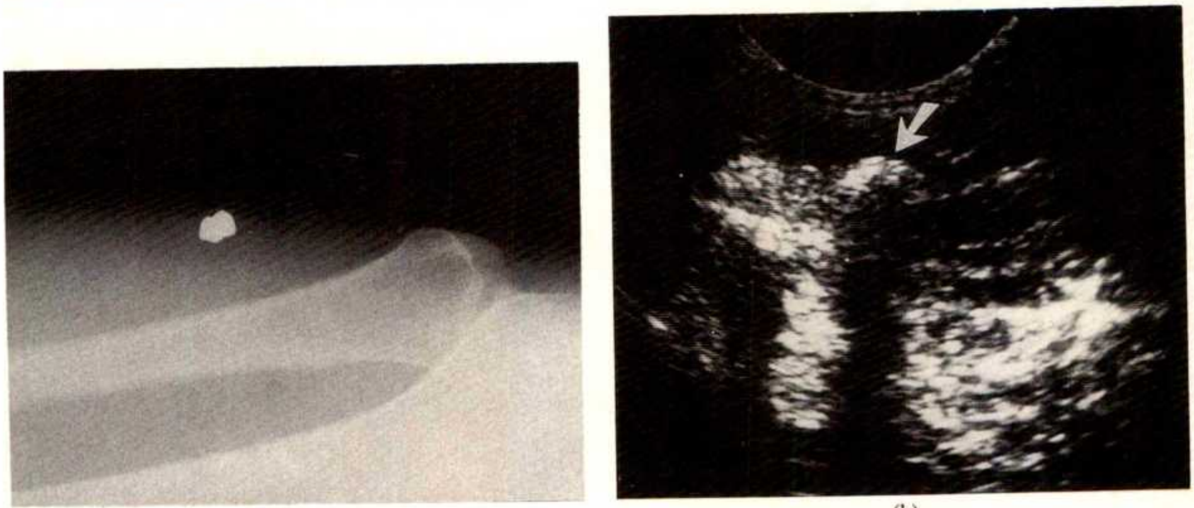

(a) (b)

Figure 2. The size and shape of an air gun pellet is clearly shown on the radiograph (a) but not with ultrasound (b) (arrow).

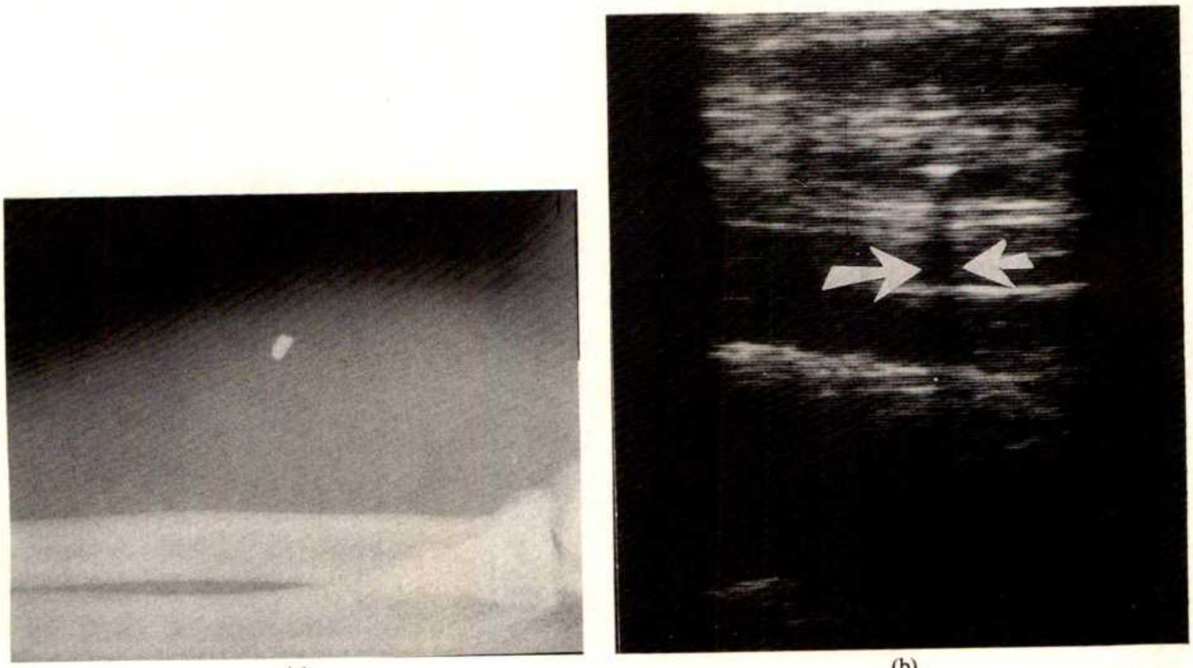
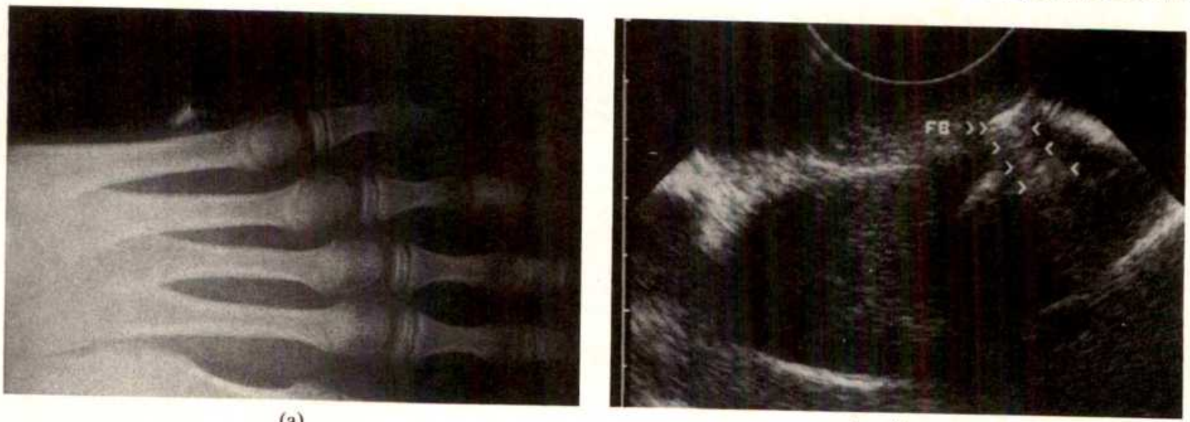

(a) (b)

Figure 3. Radio-opaque foreign body in the forearm (a) is demonstrated by ultrasound as an echo-rich focus (b). Acoustic shadowing (arrow heads) is noted distal to the foreign body.

helpful guide in the detection of foreign bodies in the soft tissue.

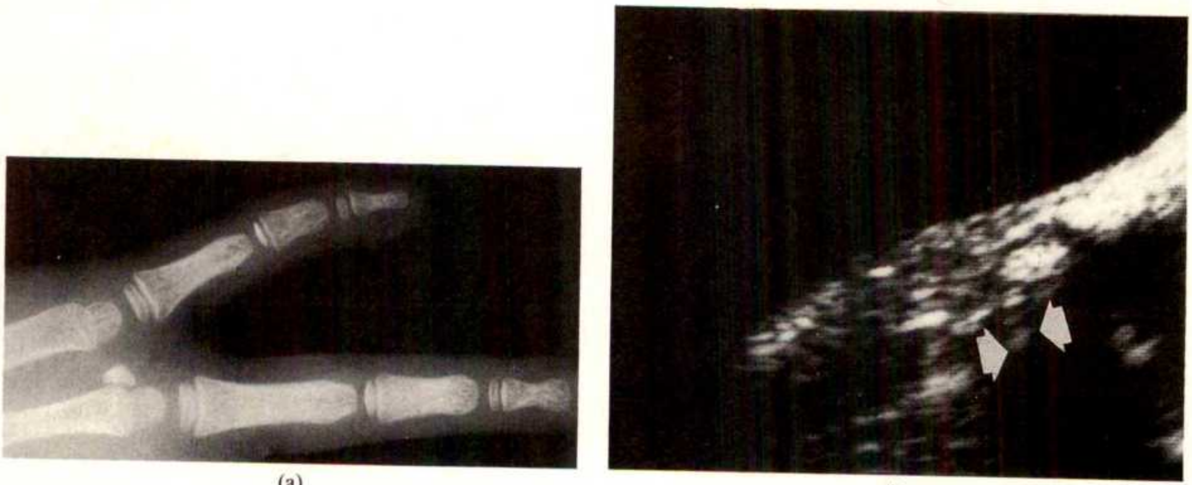
Distal to the echo-rich foreign body, in the majority of cases, acoustic shadowing is noted. This is due to the failure of ultrasound to pass through the foreign body (Fig. 3). Sometimes, instead of acoustic shadowing, distal "comet tail" artefacts may be encountered. This is due to the reverberation of sound waves on the foreign body (Fig. 4). This artefact is more pronounced with metallic foreign bodies (Ziskin et al, 1982). Occasionally, both acoustic shadowing and the "comet tail" artefact may co-exist (Fig. 5).

In our 45 patients, ultrasonic detection was found to be inaccurate in only three cases (two false positive and one false negative). In one case of radio-opaque foreign body (undetected by ultrasound), entrapped air in the



(a) (b)

Figure 4. Radio-opaque foreign body in the soft tissues of foot (a) has produced a distal "comet tail" artefact (b) (arrow heads).



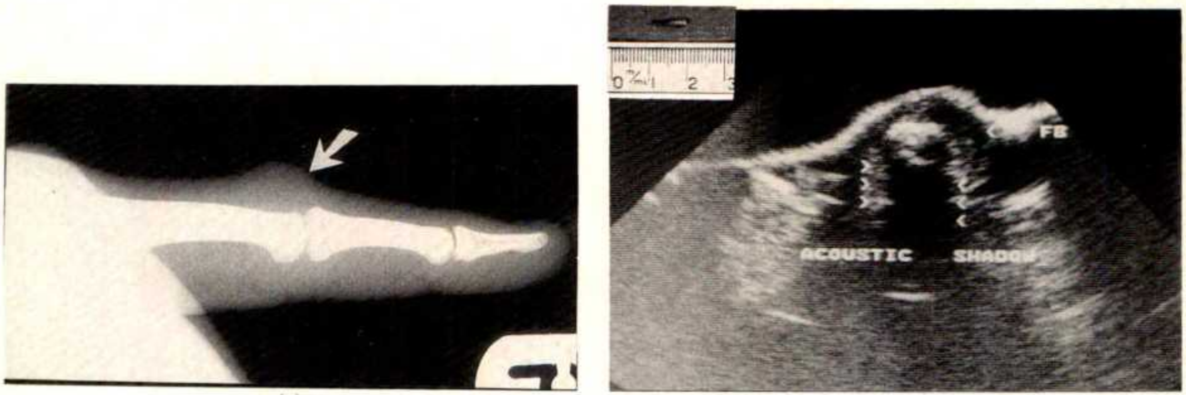
(a) (b)

Figure 5. (a) Radio-opaque foreign body in the hand (a) has produced "comet tail" artefact (arrows) and acoustic shadowing distally (b).

soft tissue overlying the foreign body had rendered the foreign body undetectable because of acoustic shadowing. In the false positive cases, calcification in soft tissue and fresh haematoma and air within the laceration were mistakenly diagnosed as foreign bodies. However, in five cases foreign bodies were correctly diagnosed by ultrasound, although conventional radiography failed to detect any foreign body in these cases.

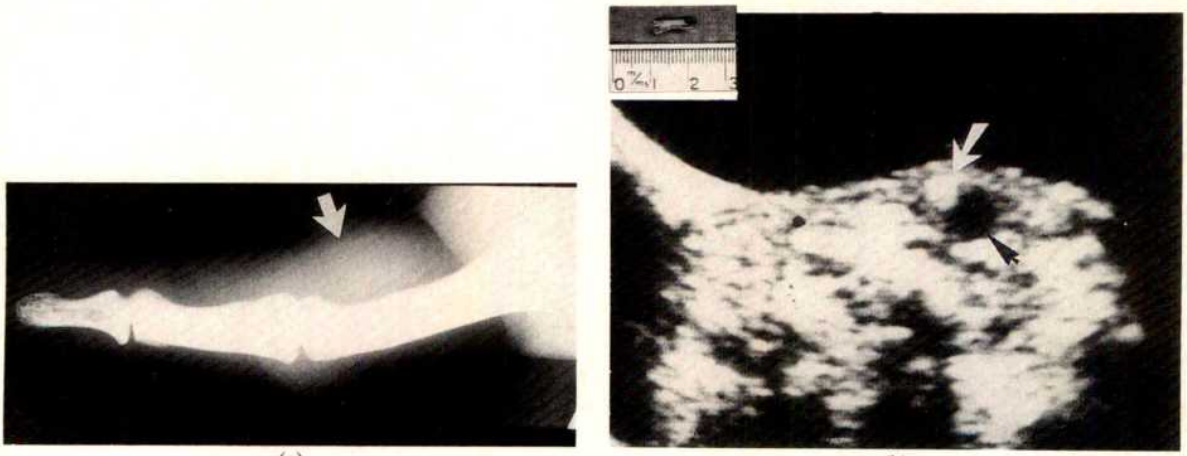
Pre-operative ultrasonic localization of foreign bodies in all three cases was found to be accurate at surgery. This study therefore indicates that sonography is a reliable method for the detection and localization of foreign bodies. However, the disadvantages should be noted. In the presence of laceration and air entrapment in the soft tissue, foreign bodies may not be identifiable. Calcific tissue and sesamoid bones may be erroneously diagnosed as foreign bodies. Large open wounds may make ultrasonic examination impracticable and the presence of fresh haematoma may be isoreflective with foreign body and thus may cause error in diagnosis. Ultrasound is time consuming and requires expertise, and 24 hour coverage may be impracticable.

The definite advantage of ultrasound is its capacity to detect radiolucent foreign bodies (Fig. 6). Even vegetable fragments such as thorns can be detected by ultrasound (Fig. 7). This has a possible clinical application, particularly blackthorn injury which is prevalent in the West Midlands and Wales. The broken end of the thorn may be retained in the soft tissue and produce severe inflammatory tissue reaction; if left for a prolonged period it may produce bone changes such as erosive arthropathy (Kelly, 1966; Southgate & Murray, 1982). These blackthorn injuries may require extensive surgical exploration for removal of the thorn.



(a) (b)

Figure 6. (a) Radio-lucent foreign body is not detected on the radiograph and only soft tissue swelling is noted (arrow). (b) A foreign body has been clearly outlined by ultrasound. Note the echo-poor area surrounding the foreign body and the distal acoustic shadowing. A wooden splinter was removed at surgery (inset).



(a) (b)

Figure 7. (a) A radiograph revealed soft tissue swelling in the ring finger (arrow head). (b) Ultrasound has outlined the thorn in cross-section (white arrow). There is a small abscess cavity surrounding the thorn (black arrow head). The thorn was removed at surgery (inset).

Pre-operative detection and localization of the thorn may be possible by ultrasound as inflammatory tissue reaction surrounding the thorn may facilitate its detection.

Lacerated skin wounds may make ultrasonic examination impracticable and may give rise to erroneous results on ultrasound. Immediate and pre-operative detection of foreign bodies in such cases should depend on plain radiography and wound exploration. However, if there is still suspicion of a retained foreign body, ultrasonic examination should be undertaken at a later date after healing of the skin. Inflammatory oedema surrounding the foreign bodies at this stage may make the foreign bodies readily detectable by ultrasound. Ultrasound is also simpler and superior to conventional fluoroscopy in the localization of foreign bodies of the extremities (Fornage & Schernberg, 1986, 1987). It obviates the need for radiation exposure of the patient and surgeon. Operating time is reduced and possible wound contamination is also minimized. We recommend that ultrasound localization should be carried out immediately prior to surgery, preferably in the operating room, as foreign bodies such as metallic needles may migrate with muscular contractions.

In conclusion, it is not advised that ultrasound should replace conventional radiography as the primary imaging technique for foreign body detection, but instead it should supplement conventional diagnostic tools, particularly when a radiolucent foreign body is suspected. For pre-operative localization, however, ultrasound can and should replace conventional fluoroscopy.

Acknowledgments

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Barium meals in the elderly—a quality reassurance

By S. P. Hawkins, MB, BS, *P. C. Rowlands, BMedSci, MRCP, FRCR and P. J. Shorvon, MRCP, FRCR

Department of Radiology, Central Middlesex Hospital, Acton Lane, London NW10 7NS, UK

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Keywords: Barium meal studies, Elderly

Abstract. The consecutive double contrast barium meal examinations of 100 elderly patients (aged over 65 years) and a group of 33 younger adult patients were analysed by two observers for technical quality and pathological abnormalities. Technical quality declined with patient age, especially in those over 75 years, but was sufficient to enable diagnosis of abnormalities in 60% of the elderly group. It is concluded that, in the majority of elderly patients, the technical quality of double contrast barium meal examinations is sufficiently high to offer considerable diagnostic utility.

During the last decade fibreoptic endoscopy has been increasingly assumed to be the best investigation for upper gastrointestinal (GI) symptoms, especially bleeding, and for the post-operative stomach (Cotton & Shorvon, 1984). In some quarters the double-contrast barium meal (DCBM) is, apparently, being ignored (Brown & Rees, 1990). However, barium studies are regarded as the best initial examination of the oesophagus and offer the advantages of simplicity for the patient, lack of sedation with return to normal activities immediately afterwards and they are safer, paticularly in patients with a pharyngeal pouch, oesophageal stricture or cardiorespiratory disease (Colin-Jones, 1986).

In the elderly, the DCBM has been said to be "often less than satisfactory" (Twining et al, 1982) owing to poor patient co-operation and frailty. Technical failures have also been identified as a cause of error (Dooley et al, 1984).

This study of 100 consecutive DCBM in elderly patients was designed to assess these assertions and to investigate the technical quality and diagnostic yield obtained.

Materials and methods

A retrospective evaluation was undertaken of 100 consecutive DCBM performed in elderly patients (aged over 65 years; mean 72 years) at the Central Middlesex Hospital between July and December 1989. A group of 33 consecutive DCBM performed during the middle of the study period on younger adults (aged 18–65 years; mean 38 years) was used for comparison. There were 53 females and 47 males in the study group and 19 females and 14 males in the younger group. The patients had been referred both by general practitioners and as hospital in- and out-patients. Patients with upper GI bleeding and previous gastric surgery were excluded from the study, as were patients for whom a dedicated barium swallow was performed.

A standard double contrast technique using EZ-HD barium suspension (E-Z-EM) and effervescent agent was used (Carbex, Ferring Pharm. Co.). At this hospital this includes single and double contrast and mucosal relief views of the distal oesophagus, and double contrast views of the stomach and duodenum. Where indicated, single contrast and compression views of the stomach and duodenum are obtained. Smooth muscle paralysis is achieved routinely using intravenous hyoscine n-butyl bromide or glucagon as appropriate and administered immediatley prior to duodenal views.

The radiographs were analysed by two experienced observers working independently and without knowledge of the age or diagnosis of the patient examined. Maximum distension in double contrast and quality of barium coating were separately scored according to a four-point scale (Table I). Ratings were given for each of the distal oesophagus, stomach and duodenum (including both the first and second parts of the duodenum). Allowance was made for films where pathology caused some loss of distension or barium coating. The diagnoses made at the original examinations were noted subsequently. Results for the study group were also analysed by division into age groups for 65–74 years and 75 years and over.

Results

The two observers' scores were closely correlated, Pearson's correlation coefficient 0.69, $p < 0.001$ (Fig. 1).

Table I. Method of scoring distension and barium coating

Score	Distension	Coating
0	Non-diagnostic	Non-diagnostic
1	Poor	Variable
2	Satisfactory, typical of good quality examination	Complete, typical of good quality examination
3	Excellent, difficult to improve upon	Excellent, difficult to improve upon

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*Current address: Department of Radiology, Royal Liverpool Hospital, Prescot Street, Liverpool.

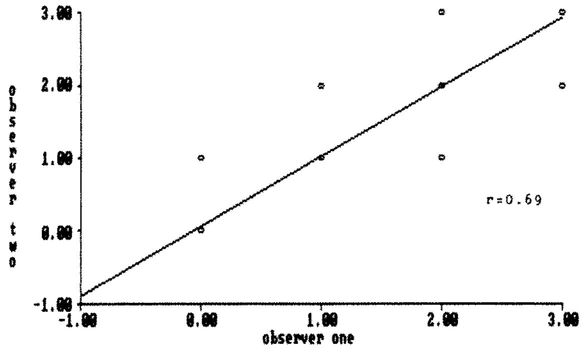

Figure 1. Correlation of observers for all parameters in 133 patients.

The mean assessment scores of the two observers are shown in Table II. The young group showed better than satisfactory ratings (> 2.00) for all parameters except oesophageal and duodenal coating (1.86 and 1.94, respectively) which were near to satisfactory. The elderly group showed deterioration in technical quality overall, particularly in the group of over 75-year-olds. However, only 51 of the total of 600 ratings were given by one or both observers as non-diagnostic. Three-quarters of non-diagnostic scores were for oesophageal and duodenal coating, and except for these areas all parameters were graded 1.50 (mean) or above even in the group of over 75-year-olds.

The clinical indications for the request of a barium meal are shown in Table III. The diagnoses recorded for the control and elderly groups are shown in Table IV.

Discussion

There has been little attention to the utility of barium meal examinations in the elderly. Such patients often provide a technical challenge to the radiologist owing to immobility and frailty. However, they are also a group in which cardiovascular disease is common and the majority of complications during endoscopy involve the cardiovascular system (Bell, 1990).

Our study has shown that the technical quality of barium meal examinations declines with the increasing age of the patient. In those over 75 years old the quality of barium coating for double contrast views in the distal oesophagus and duodenum is poor. This may lead to diagnostic error if only a double contrast technique is used. At this hospital both single contrast and mucosal relief views of the distal oesophagus are obtained routinely during a DCBM, and single contrast and compression views of the stomach and duodenum if indicated. The quality of these views is more difficult to grade and they were excluded from the study. Apart from the coating problems in the oesophagus and duodenum, the other technical factors that were assessed gave results approaching that of a good quality examination (considered satisfactory even in younger patients).

This study did not aim to suggest that DCBM can be used as the sole investigation of the upper GI tract in any age group. The sensitivity and specificity of endoscopy is greater (Dooley et al, 1984) and endoscopy provides the facility of biopsy. However, these authors conclude that if a DCBM (with a specificity found to be 91%) reveals a lesion that accounts for the patients' symptoms then it should be treated. Indeed, current radiological technique is better at showing certain functional aspects, hiatal hernias and extrinsic compression (Cotton & Shorvon, 1984). Unnecessary duplication of examinations should be avoidable (Colin-Jones, 1986).

Our study found pathological abnormalities in 60% of elderly patients (and 40% of the younger group); this is comparable with the 67% of abnormalities found in a study of the elderly at upper GI endoscopy (Lockhart et al, 1985). When pathology is found at DCBM, or if no pathology is found and clinical suspicion is high, a low threshold should be maintained to proceed to endoscopy and biopsy. This is particularly relevant for oesophageal and gastric lesions. Referral for endoscopy was the commonest management change following barium meal in a study of elderly patients (10 patients of 36 management changes in 101 patients examined) (Twining et al, 1982).

The relative indications and safety of each investigation have been considered previously (Ansell, 1987; Arfeen et al, 1987; Simpkins, 1988).

We conclude that, if sufficient expertise and experience is available, elderly patients, even if frail, can undergo a barium meal examination of reasonable quality and diagnostic confidence in a large majority of cases.

Table II. Mean assessments of both observers

	Young (under 65 years) $n = 33$	Elderly (over 65 years) $n = 100$	Elderly (65–74 years) $n = 72$	Elderly (over 75 years) $n = 28$
Oesophageal distension	2.20	1.90	1.95	1.76
Oesophageal coating	1.86	1.58	1.72	1.18
Stomach distension	2.33	1.95	2.00	1.80
Stomach coating	2.19	1.70	1.78	1.50
Duodenal distension	2.20	1.82	1.86	1.71
Duodenal coating	1.94	1.45	1.53	1.25

Table III. Indications for barium meal

	Young $n = 33$	Elderly $n = 100$
Epigastric pain	32	75
Heartburn/reflux	1	5
Cachexia	0	9
Iron deficiency anaemia	0	4
Early satiety	0	2
Others	1	8

Table IV. Diagnoses for young and elderly groups

Diagnosis	Young $n = 33$ (%)	Elderly $n = 100$
Normal	20 (60)	40
Oesophageal reflux	7 (21)	25
Hiatus hernia	0	23
Oesophageal stricture (benign and malignant)	0	6
Oesophagus others	0	4
Gastritis	1	1
Gastric ulcer: benign	1	2
malignant	0	7
Gastric polyp	0	4
Linitis plastica	0	1
Stomach others	1	0
Duodenitis	1	0
Duodenal ulcer	4 (12)	14
Duodenum others	1	0

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A new phantom for mammography

By J. Law, PhD

Department of Medical Physics and Medical Engineering, Edinburgh University and Western General Hospital, Edinburgh EH4 2XU, UK

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Keywords: Mammography, Phantom

Abstract. A new mammography phantom from Du Pont is described. It has a wider range of types of detail than in previous phantoms, including some which closely simulate breast tissues. Experience of its use, and comparisons with an earlier ("Barts") phantom, are reported. The Du Pont phantom appears to have greater sensitivity to changes in tube kV and focal spot size, and better discrimination between different film–screen combinations and between films from different breast screening centres.

The importance of a suitable phantom, or test object, in monitoring and maintaining image quality in mammography is well known (see for example Pritchard, 1988). Such a phantom should contain details which mimic those which a radiologist looks for in clinical mammograms, and may also contain means for assessing limiting contrast and resolution. These two approaches are quite distinct, since many clinical details depend on a combination of both contrast discrimination and resolution. If the latter are assessed separately, it is not always a simple matter to combine the results to give a single measurement with an obvious relationship to the radiologist's needs.

It is even more important that films of a phantom show clear differences if tube kV, focal spot size, or film/screen/processing characteristics change, especially since these may drift gradually. In screening mammography in particular, a useful phantom should be able to demonstrate such drifts before they become apparent in clinical mammograms. (Even if a phantom does not do this, it may still have a role in identifying the origins of such drifts.)

One phantom which adopts the first approach is that described by White and Tucker (1980) and sometimes called the "Barts" phantom. This has been extensively used in a limited number of UK centres and found very valuable in at least some. However, it was difficult to construct, was never available commercially, and is no longer obtainable. It is also only moderately sensitive to changes in kV (Law et al, 1989) and, at least for contact films, shows little sensitivity to changes in focal spot size. A more sensitive replacement has been needed for some time, but until very recently only one other phantom has shown any clearly demonstrable improvement, and some have failed to match it. That exception was the Wisconsin randomized phantom, which is too time consuming for routine use. This paper describes results obtained from a new phantom with a variety of types of detail, marketed by Du Pont. It appears to have most of the features outlined above.

Description of phantom details

The details are contained within a "black box" measuring approximately 10 cm × 8 cm × 2 cm. This can be placed in various ways within an assembly of different sized pieces of Perspex, which all together simulate a compressed breast of average size.

The details are shown in Fig. 1. They include various objects with a range of contrasts, which mimic clinical mammographic features and which lend themselves to quantitative scoring, plus seven line bar patterns in two directions at right angles, from 8 to 20 lp/mm at low contrast, in steps of 2 lp/mm, which can also be counted to give a resolution score. In addition, there is a range of simulated tissues and structures, much more like breast tissue than any of the other features, but which are difficult to score except qualitatively or on a scale of (say) 1 to 3. Lastly, over small areas the line bar patterns at right angles to each other overlap to give an indication of point resolution.

The objects having a range of contrasts are of four kinds, and each is provided in five decreasing sizes and contrasts. These are:

(a) Al_2O_3 specks from 320 to 83 μm which mimic microcalcifications;
(b) plastic wires from 0.8 to 0.3 mm which mimic fibrous structures;
(c) carbohydrate or amino-acid spheres from 1.2 to 0.35 mm;
(d) discs containing 0.8 mm diameter holes, arranged to form the single digits 7, 5, 4, 3 and 2, where each digit indicates the depth of the holes.

The simulated breast tissues are provided in three clusters of four each, which have very low, low, and normal absorption. Many also contain random microcalcifications. There is also a single sample about 2 cm in diameter representing the appearance of "dense breast", and some small fine structures said to represent lymph nodes.

Methods of use of phantom

The arrangement recommended by the manufacturers has been used to obtain the results which follow (Fig. 2). One piece of Perspex, 12 cm × 12 cm and 3 cm thick, is placed directly on the grid cover at the patient side, and with the 10 cm × 8 cm "black box" on top of this. The 4 cm space to one side of the box is partly filled by another Perspex piece, 12 cm × 3 cm × 1 cm,

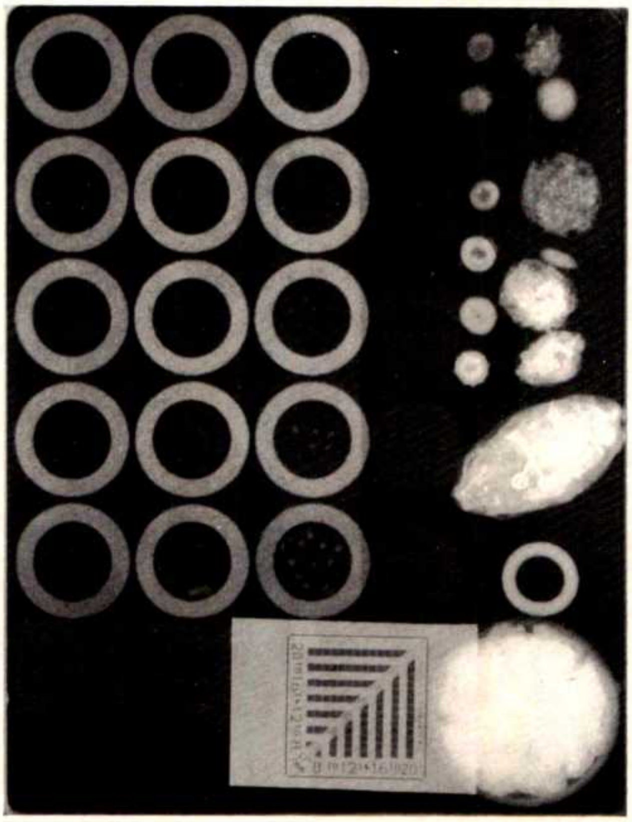

Figure 1. Radiograph of phantom with minimum of scattering material.

and a further Perspex piece 12 cm × 12 cm × 1 cm is placed above this and the black box. Thus the total attenuation is about 5 cm Perspex. Behind this assembly, *i.e.* away from the patient, a Perspex step wedge can be placed, transverse to the anode cathode direction now normal in mammographic tubes. This wedge has eight steps from 5 to 40 mm, and may be placed on top of another Perspex piece, 12 cm × 3 cm × 1 cm, if desired. Lastly, the compression plate is lowered onto the whole assembly.

To "score" the films, *i.e.* to obtain a numerical figure of merit with some relationship to image quality, the manufacturers make no recommendations and numerous methods might be derived. To obtain the results reported here, the following method was adopted. For the four types of feature (a) to (d) above, each of the five sizes was given one point if it could be seen quite clearly, with edges appearing sharp to the eye, and half a point if some features of the type concerned were unambiguously visible but less clear. Doubtful appearances were given no score. This scoring was helped initially by a radiograph of the "black box" with no Perspex or other scattering material adjacent. Radiologists' binocular viewers were always used to cut out surrounding glare.

Secondly, the line frequency plainly resolvable in each direction was recorded using a three-lens viewer

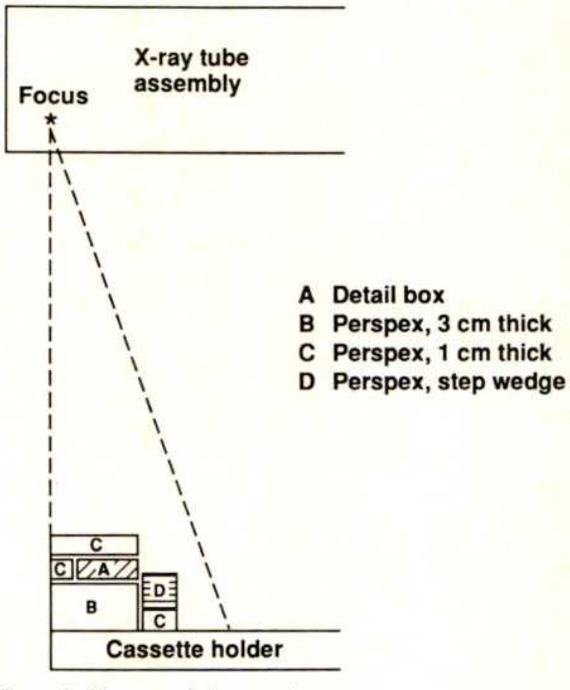

Figure 2. Diagram of phantom in use.

Table I. Image scores at Centre A for various tube kV and focus sizes, and for magnification films (× 2.0)

Tube kV	Contact films		Magnification films
	Broad focus 0.6 × 0.5 mm	Fine focus 0.14 × 0.11 mm	Fine focus 0.14 × 0.11 mm
(a) *Contrast details counted/line pairs per mm resolved (see text). Results averaged for two scorers*			
25	16.25/13	14.25/13	18.0/17
28	14.25/13	—	—
30	13.5/11	13.0/12	17.25/17
32	12.75/11	—	—
35	12.25/9.5	11.25/12.5	15.5/14.5
(b) *Breast tissue structures scored by radiologist on scale of 1 (poor) to 3 (good), or 1 to 5 for dense breast*			
25	14	10	13
28	10	—	—
30	10	10	13
32	9	—	—
35	6	9	9

Table II. Image scores at centre B for various tube kV and focus sizes; contrast details counted/line pairs per mm resolved (see text); contact films

Tube kV	X-ray set 2	X-ray set 3	
	Broad focus 0.96 × 0.84 mm	Broad focus 0.37 × 0.47 mm	Fine focus 0.12 × 0.10 mm
25	11/8.5	12/11.5	14.5/14.5
28	11.5/8.5	11.5/12	14.5/14.5
30	11/8.5	11.5/12	12.5/13.5
32	9.5/8.5	10/12	9.5/8.5
35	—	9/11	10/13.5

provided with the phantom. Where lines could be distinguished over part but not all of the next bar, that frequency minus 1 was taken as the limit. The resulting line frequencies in the two directions were then averaged.

In some films the simulated tissues were also scored, mostly on a scale of 1–3, but using 1–5 for the "dense breast" feature. This scoring was only attempted by a radiologist, and on only a few of the films.

Experimental results

The phantom was radiographed in the arrangement described above, using a range of tube kV on each of three different X-ray tubes, two of which had dual foci. These three X-ray sets were in two different centres. Secondly, at selected kV on two of these tubes in one centre, results were obtained for three very different focal spot sizes. Thirdly, on one tube using broad focus and 28 kV, a variety of film–screen combinations was used, including several which were thought to be good and at least some known to be poorer. Lastly, the phantom was used on seven screening or assessment units in three Scottish centres, using local films, screens and processing. For all these films, the scores were compared with those of the Barts phantom under similar or identical conditions.

Effect of changing tube kV

In centre A, using X-ray set no. 1, tube kV was varied from 25 to 35. Exposures were made under automatic exposure control to obtain densities which were reasonably uniform within the range 1.0–1.4. Films were scored by a physicist and a radiologist; the latter's scores were higher but the difference was approximately constant and the results were combined in Table I.

In centre B, similar films were obtained on X-ray sets 2 and 3 and scored by the physicist. Results are given in Table II. At this centre two Du Pont phantoms were available for a time, neither of which had been at centre A. This experience with three of the phantoms confirmed that no significant differences were likely to arise between different specimens of this phantom design.

Effect of changing focal spot, and of magnification

The sizes of the foci are given in both Tables I and II. In centre B these sizes were measured by both slit and star resolution techniques and the results averaged. In centre A similar measurements were made by different staff, and the magnification was nominally 2.0 in both centres.

Variation of film–screen combination

Six different combinations were used in centre B on X-ray set 3. These were chosen to include some of the best performers in tests with the Barts phantom and also some others for which results had been significantly worse. All these films were obtained using black plastic evacuated envelopes, at 28 kV with grid on broad focus. The results are given in Table III, which combines results from physicist and radiologist. For Tables III and IV, results from three films obtained under identical conditions were summed to reduce random errors.

Table III. Image scores at centre B for various film–screen combinations; X-ray set 3 at 28 kV, broad focus

Film–screen combination	Barts phantom[a]	Du Pont phantom	
		Contrast details[b]	Line pairs/mm
A	57.0 ± 0.2	43.3	14.5
B	56.9 ± 0.4	42.3	13.0
C	55.9 ± 0.5	40.8	14.2
D	53.8 ± 0.8	39.5	13.6
E	53.1 ± 0.8	36.5	13.0
F	48.9 ± 0.6	27.8	11.0

[a] Means of sets of six films each, with standard errors.

[b] Sums of scores from sets of three films each, averaged for two scorers.

Table IV. Image scores from three centres and seven X-ray sets; local films, screens, cassettes and processing

Centre	X-ray set	Magnification	Barts phantom[a]	Du Pont phantom	
				Contrast details[b]	Line pairs/mm
B	2	—	53.7	33.5	9.0
D	8	—	55.7	33.5	12.8
C	5	—	55.9	37	12.0
C	6	—	56.1	32	12.5
B	3	—	56.3	36.5	11.5
B	4	—	57.5	40	13.0
D	7	—	57.9	40	12.8
C	6	Yes	58.9	43	15.6
D	7	"	59.7	46.5	14.4
B	3	"	59.9	48	12.7

[a] Means of sets of six films each.
[b] Sums of scores from sets of three films each.

Comparisons between other centres

Both the Du Pont and the Barts phantoms were used at three different centres on the same days, and on a total of seven different X-ray sets. Local films, screens, cassettes and processing were used in each case, and this included four processors, and three film–screen–cassette combinations. Results from both phantoms are given in Table IV, where the scores were those of the physicist alone.

Discussion

Results shown in tables

In Tables I and II there is a steady fall in image score, both for contrast details and for breast tissue structures, as tube kV rises. This decrease is proportionately greater than with the Barts phantom in earlier work (Law et al, 1989). In Table II there is a marked increase in resolution in contact films as the focus size decreases. This effect is predictable on geometrical grounds but has not yet been clearly reported for the Barts phantom. In Table I, this effect is not seen in contact films, but with magnification there is a marked increase in image scores both for contrast details and for resolution, again proportionately greater than has so far been shown with the Barts phantom.

In Table III, the relationship between score from the Barts phantom and resolution in the Du Pont phantom is moderately close, but with the contrast detail score it is much closer. These results are shown in Fig. 3. Again, the Du Pont phantom appears to be more sensitive, that is it discriminates more clearly between different film–screen combinations. In addition, the closeness of the points to the line in Fig. 3 supports the reliability of results obtained with either phantom. A somewhat similar correlation between the Barts and Wisconsin phantoms was shown in earlier work (Kirkpatrick & Law, 1987). In Table IV and Fig. 4 the relationship between results with the two phantoms is not quite so close, but the discrimination shown by the Du Pont phantom appears even greater.

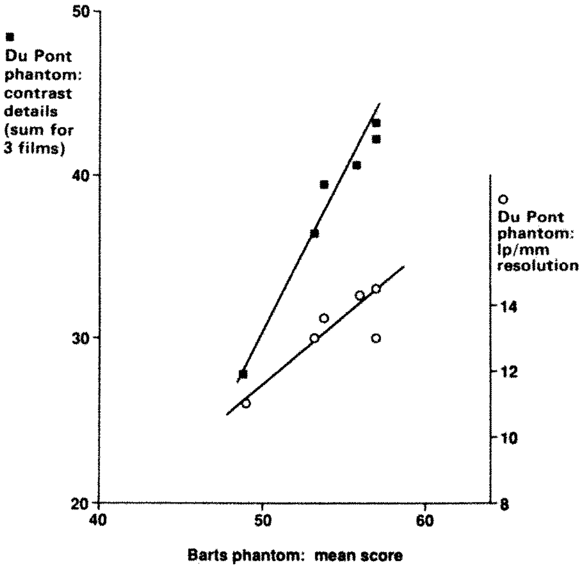

Figure 3. Phantom scores from different film–screen combinations.

Miscellaneous considerations

As well as showing greater discrimination than the Barts phantom, the Du Pont phantom has been shown to do this with only three films for each set of conditions

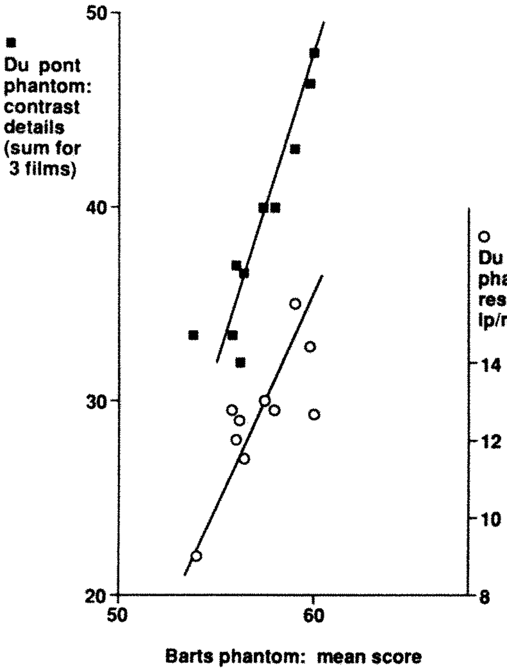

Figure 4. Phantom scores from different centres.

rather than six as currently used by the Barts. These films were also found to be quicker to score. Moreover, staff have found it much quicker to learn to score with the Du Pont phantom than with the Barts. This has been found for a physicist, a radiologist, a radiographer and a technician, and regardless of past experience of film scoring with other phantoms. Thus it promises to be more convenient and reliable to use.

The scoring systems described here are still provisional. Consistency of scoring for any one user or group of users is essential, and users may need to develop whatever system suits them best. Consistency of scoring between different users or centres is also desirable, especially if a type of phantom is widely used, but a phantom may still be of great value even without this.

Conclusion

When choosing a new mammographic phantom, the user must be satisfied that it is more sensitive to drifts in exposure conditions, or more discriminatory between different imaging systems, than those in current use. The Barts phantom, valuable though it has been, has suffered from having only moderate sensitivity unless many films are taken, and from not being readily obtainable. Other phantoms which are available have been tried from time to time but none has so far shown sufficient sensitivity or discrimination to replace it. The new Du Pont phantom has been found to have better sensitivity and discrimination, combined with speed and convenience in use and scoring, and is currently available. Several have been ordered for use in the Scottish Breast Screening Programme.

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I am grateful to Dr Alice Underwood of the Department of Medical Physics, Weston Park Hospital, Sheffield, for drawing my attention to this phantom. She and Mr Alan Robinson kindly allowed me to see some of their films of it, and to obtain others for my own use on an X-ray set in their Region. I am also grateful to Du Pont for giving me the use of two more phantoms in Scotland. Lastly, I must acknowledge the help I have received in film scoring and by constructive comments from D. A. E. Kirkpatrick, Dr B. B. Muir, Mrs Joyce Coupar and Miss Dorothy Shaw.

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Carcinoma of the breast: measurement and the management of treatment

II. The regression of tumours

By *C. W. D. Cheung, MSc and A. E. Johnson, FRCS, FRCR
Breast Study Centre, Mount Vernon Hospital, Northwood, Middlesex, UK

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Abstract. Regression slopes fitted in 238 new cases of primary breast cancer submitted to a variety of managements are analysed. Contrary to the original hypothesis that slopes would primarily reflect the composition of the tumours, the steepness of resorption slopes is found also to be treatment dependent. Investigation of other factors influencing slopes is confined to radiotherapy where the expectation that the prescribed dose will be delivered is high. A large cumulative radiation effect before the start of shrinkage is associated with steeper slopes. A small correlation between slope and both menopausal status and starting diameter has been found, with premenopausal patients and small tumours producing the steepest slopes. The full range of slopes has been seen in postmenopausal patients. The data has been fitted to a linear model to evaluate the relative importance of these associations. Illustrative cases support the hypothesis that resorption slopes are a product of tumour architecture and histology but we conclude that the maximum possible steepness of slope is not always achieved in the clinic, even when radiation is used. A combination of histological and regression data is therefore required to characterize a tumour for predictive purposes.

We have presented the statistical validation of a method of estimating the changing volume of breast cancers in response to treatment using engineers' callipers (Cheung & Johnson, 1991). As indicated in that paper, our hypothesis is that we should be able to identify one characteristic resorption slope for each individual tumour, irrespective of the mode of treatment.

Exponential regression lines have been fitted to the data by the method of weighted least squares and classified according to their steepness and the associated treatment. ("Regression" is used in the statistical sense to include both tumour resorption and accretion.) We now consider the interpretation of these lines in relation to our hypothesis. We have again used the SAS package† for the CRC Gray Laboratory MicroVAX computer in our analyses and, where not otherwise specified, the cut-off level for significance is taken as $p < 0.05$.

Patients and treatments

The measurement technique may be evaluated in any tumour, whereas only primary breast cancers, for which no previous therapy has been given, should be considered in the analysis of the relationships between slopes and factors which may influence them. The five patients whose data did not support a significant resorption slope were also, perforce, excluded. There were 24 exclusions (Tables I and II) from the original 262 patients whose data was analysed in our previous paper (Cheung & Johnson, 1991). The mean age, 60 years, and the geometric mean diameter, 46 mm, are unchanged for the remaining 238 patients. The age distribution is still normal. The distribution of starting sizes has the same range but an increase in the proportion of tumours under 30 mm in diameter is seen. The proportion of patients in each menopausal category is similar: 38 premenopausal (16%), 178 postmenopausal (75%) and 22 perimenopausal (9%).

The patients are grouped in temporally overlapping series according to the first management (Table II). The first patients were treated by external beam radiotherapy, sometimes combined with radium implantation, according to the standard practices of four radiotherapists (Table III). During this early period, 15 patients receiving standard combination chemotherapy or hormones as their first treatment by colleagues were also measured. Meanwhile, neo-adjuvant chemotherapy had been introduced in collaboration with Dr Paul Strickland in 1975. The first eight patients so managed received up to three doses per week of a mixture‡ of cytotoxic drugs before planned radiotherapy. The effectiveness of this preliminary treatment in shrinking the tumours prompted an attempt to achieve the maximum benefit from the drugs before irradiation. The next 15 patients were given "the mixture" weekly for up to 5 weeks and then twice monthly in a "Belfast" type of timing (Edelstyn et al, 1975) to allow recovery from

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* Present address: CRC Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex.
Address for correspondence: Dr A. E. Johnson, Breast Study Centre, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN.

†SAS: Statistical Analysis Systems Institute Inc.

‡ "The Mixture" was 1000 mg fluororacil, 500 mg cyclophosphamide and 1 mg vincristine intravenously, followed by 2.5 mg × 3 oral methotrexate over the next 24 hours.

Table I. Reasons for exclusion from later analyses

Tumour factors	
Regrowth after local excision	5
Local recurrence after mastectomy	3
Secondary deposit in remaining breast	3
Measurement factors	
No significant resorption slope	5
Treated "growth" faster than resorption	2
Treatment elsewhere before measurement	6
Total	24

Table II. First managements with exclusions

First treatment	Total	Exclusions	Final
Radiotherapy	75	7	68
Other systemic treatment first	19	4	15
Mixture up to three times	8	0	8
Mixture to failure	16	1	15
Mixture without methotrexate to failure	11	0	11
Fluorouracil to failure	19	0	19
MBST first	114	12	102
Total	262	24	238

The final column contains those patients whose data is subjected to further analysis.

bone marrow depression resulting from the early intensive treatment. A further 11 patients had "the mixture" without the oral methotrexate, the absorption of the latter being uncertain because of vomiting after the injections. A final group of 19 patients received the single agent fluorouracil (1000 mg per week intravenously) to failure; all tumours enlarged again sooner or later and were then irradiated. The survival of these patients is very poor, but where local recurrence was a problem in the long term a few patients have had salvage surgery.

From 1979 onwards, 102 unselected new patients representing all stages of the disease were treated in the Breast Study Centre by sequential courses of single agent intravenous chemotherapy consisting of 600 mg/m^2 fluorouracil, 300 mg/m^2 cyclophosphamide, 1 mg vincristine, 15 mg/m^2 methotrexate or 15 mg/m^2 doxorubicin (or latterly 3 mg/m^2 mitozantrone) once weekly for 4 weeks, together with continuous hormone therapy, which was started after the first course of injections, using 40 mg tamoxifen daily. Where tamoxifen was shown to be ineffective, oestrogens, androgens or progestogens were tried in the appropriate age groups. Fluorouracil was the first drug in 63, methotrexate in 14, mitozantrone in 20 and cyclophosphamide in four cases, respectively; vincristine was the first drug only once. The original choice of fluorouracil as the first treatment was arbitrary. When we perceived the importance of the first drug in relating slopes to treatment (*vide infra*), we changed the sequence of drugs. It was then too late in the series to accrue useful numbers for methotrexate, cyclophosphamide or vincristine. The timing of treatments was controlled by measurement of the primary tumour: measurement based sequential therapy (MBST). The intervals between courses of chemotherapy ranged from 1 to 6 weeks according to progress and, once established, the volume halving time (vht) of the tumour. The preferred final local management in these MBST patients was local excision of the residue together with node biopsy, followed by external beam radiotherapy to the breast and to the nodal areas if indicated; mastectomy, with or without post-operative radiotherapy, was performed where local excision was inappropriate. Radiation alone as the final management was reserved for palliation where survival was expected to be short because of metastatic disease (four patients whose tumours were inoperable but who were without overt metastases, received radical radiotherapy).

The clinical management and results will be presented in a later paper; we are here concerned with the interpretation of the regression lines, upon which treatment direction depends.

Resorption

Where possible, regression lines have been fitted in relation to distinct treatments (Fig. 1) but in some cases, particularly in response to MBST, a steady shrinkage was observed during a sequence of different medications (Fig. 2). Any individual patient seldom produced slopes

Table III. Radiotherapy treatment schedules

*cGy	Days	Fractions	D/F	CRE	Comment
6500	44	32	203	1865	
6000	35	25	240	1874	Sometimes 2000 cGy electron "top up"
5500	37	27	204	1679	
3885	21	15	259	1451	+ Ra implant 4000 cGy/4 days or + 2000 cGy 250 KV in 10 fractions to reduced volume

* Primary treatment ^{60}Co γ rays; 8 MeV linear accelerator used for large patients and for electron treatments.
D/F = dose per fraction; CRE = cumulative radiation effect.

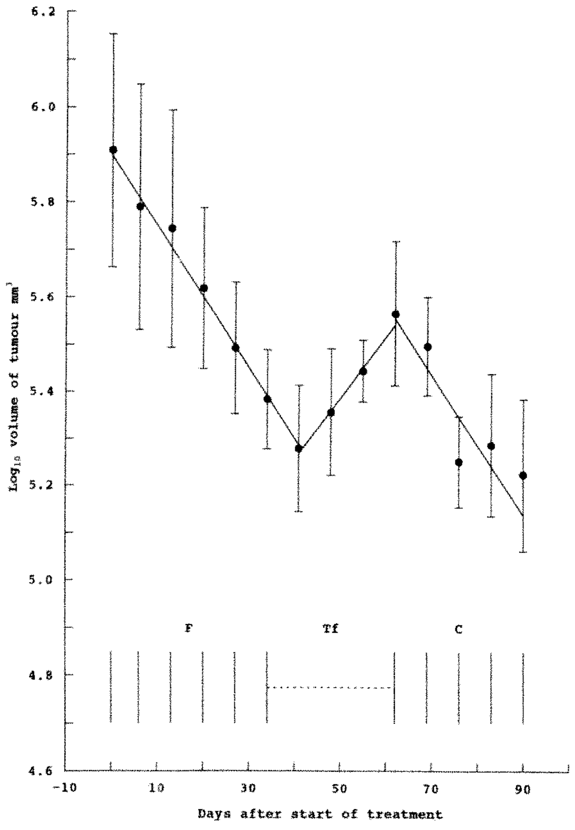

Figure 1. Regression slopes fitted in relation to fluorouracil (F), tamoxifen (Tf) and cyclophosphamide (C).

that were all parallel (Fig. 3) and we have to account for this diversity of slopes at different times in the course of the treatment of a single patient.

This variety of slopes is not susceptible to statistical analyses because all later slopes must be dependent upon the earlier ones, but slopes resulting from the first treatment might be regarded as typical of the unperturbed tumour. A summary of these is shown in Table IV. In 12 cases there was no significant regression slope in response to the first management and five tumours enlarged significantly, although resorption slopes were produced by later treatments. From the remaining 221 first resorption slopes the following groups were large enough to be analysed according to their treatment: radiotherapy (68), "the mixture" (28), fluorouracil (45), fluorouracil with tamoxifen (13), mitozantrone (10) and MBST (27). These groups cover 191 of the first resorption slopes shown in Table IV; their general characteristics are presented in Table V. First treatment slopes will be attributed to MBST only if the first chemotherapy or chemotherapy followed by hormone does not lead to the fitting of a separate slope.

Natural log transformation of the slopes was made. The natural logarithms of the slopes provided the most convenient numerical range for presentation of the statistical results, whereas, historically, $\log_{10}$ had been used in graphical presentation. As there was a range of standard errors, individual slopes were weighted by the reciprocal of their coefficient of variation before calculating the mean for each treatment group. A one-way analysis of variance then showed that a significant difference existed between the mean natural log slopes associated with the six subsets ($F = 12.08$ $p < 0.0001$). Further to distinguish the mean natural log slopes, Duncan's Multiple Range Test was applied (Duncan, 1955). This test extends the F-test from the significance of the overall difference to that of the difference between individual means. The results confirm that significant differences exist between most of the mean natural log slopes, with overlap within the single agent chemotherapies fluorouracil and mitozantrone where the means are indistinguishable. Figure 4 shows the mean natural log slopes, with their 95% confidence limits, according to the treatment applied.

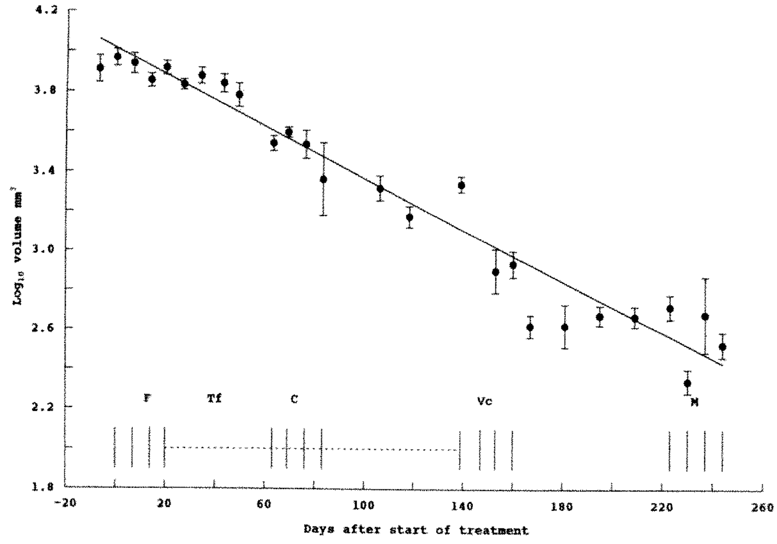

Figure 2. Resorption slope attributable to MBST style of management. Vc = vincristine; M = methotrexate. Discontinuation of tamoxifen at Day 140 was premature in that the apparent enlargement was produced by the absence of the observer whose measurements were consistently smaller than the others. Tamoxifen was later reinstated successfully.

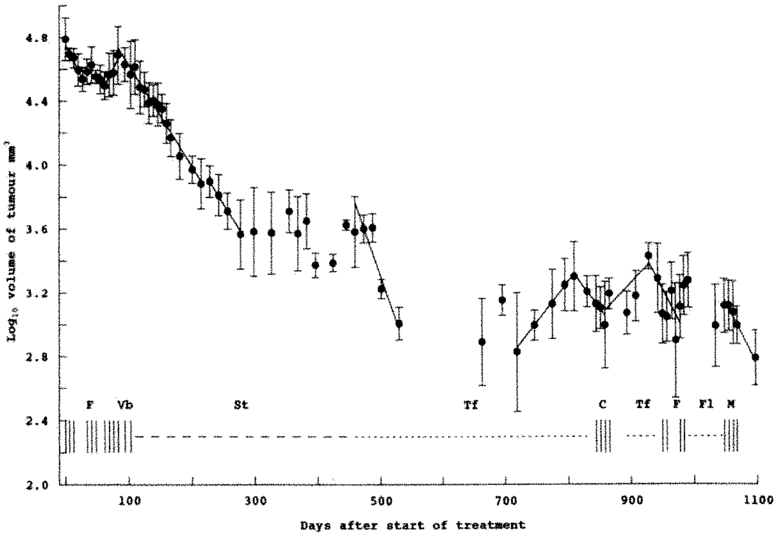

Figure 3. Slopes typical of a long time course. Vb = vinblastine; St = stilboestrol; Fl = fluoxymesterone.

Table IV. Details of slopes attributable to first managements

Treatment	Patients	Slopes	Resorption	"Growth"	No significant slope
Radiotherapy	68	68	68	0	0
"Mixture"	30	28	28	0	2
"Mixture"/RT	4	4	4	0	0
Standard systemic					
Hormone	5	5	5	0	0
Hormone and chemotherapy	3	3	3	0	0
Mix + dox.	7	7	7	0	0
Fluorouracil	82				
Alone		47	45	2	7
+ Tf		13	13	0	0
In MBST		14	14	0	0
In other		1	1	0	0
Methotrexate	14				
Alone		4	4	0	1
+ Tf		1	1	0	0
In MBST		7	6	1	0
In other		1	1	0	0
Mitozantrone	20				
Alone		12	10	2	1
In MBST		7	7	0	0
Cyclophosphamide	4				
Alone		2	2	0	1
+ Tf		1	1	0	0
Vincristine	1	1	1	0	0
Total	238	226	221	5	12

"Mixture"/RT = single slope from radiotherapy with preceding "mixture".
Mix + dox. = mixtures containing doxorubicin.
+ Tf indicates that the preceding chemotherapy slope was indistinguishable from that resulting from the tamoxifen which followed.
In MBST = slope attributable to sequence of drugs and hormones beginning with the named drug.
The total for MBST is the sum of the separate entries.

Table V. Characteristics of first treatment groups

Treatment	Number of patients	Mean slope (geometric)	Mean age	Mean diameter (geometric)	Menopausal status (%)		
					Pre-	Peri-	Post-
Radiotherapy	68	−0.0180	58	56	19	16	66
Mitozantrone	10	−0.0133	70	31	0	10	90
Fluorouracil	45	−0.0128	63	41	6	6	87
Mixture	28	−0.0100	58	69	29	4	68
F + tamoxifen	13	−0.0080	66	36	8	0	92
MBST	27	−0.0046	60	30	11	7	82

This variation of the steepness of the mean natural log slopes according to treatment and the absence of a significant resorption slope in response to the first treatment in 17 cases led us to try to define a representative slope for each tumour, to be chosen as the steepest significant resorption slope. The division of the representative slopes according to treatment is shown in Table VI. In Fig. 5, the distributions of slopes resulting from all first treatments, representative slopes and slopes resulting from radiotherapy as first treatment are compared. The implication of this graph is that "representative" slopes are not necessarily truly representative if radiotherapy has not been given. One hundred and ninety-two of the representative slopes were either first treatment slopes or one of a set of parallel slopes which included the first slope.

The mean resorption slopes have also been calculated in relation to all treatments (both first and subsequent), all first treatments, representative slopes for each patient and all first radiotherapy slopes (the first slope in response to this mode of treatment in any part of the time course) as well as representative slopes resulting from radiotherapy. The position of these means in the spectrum of slopes related to treatments is indicated in Fig. 4. Tests of significance are not applicable, since some slopes appear in more than one grouping and not all apply to first treatments.

The investigation of possible associations between treatment and slope cannot be extended to subsequent slopes because of the dependence of the later slopes upon earlier management. We have a clear example of this for mean slopes resulting from "the mixture", for which a relatively shallow mean natural log slope was found when it was the first treatment. (This may be related to the large size of the tumours: *vide infra.*) In the case of some later patients managed by MBST, where slow shrinkage was seen in the presence of poorly differentiated histology, we changed to the combination chemotherapy of "the mixture" and then saw steeper slopes. The mean slopes for the later mixture are therefore steeper than earlier ones as a result of clinical selection.

No clear statement regarding the relationship of growth to resorption slopes can be made from this data. We measured only 19 slopes reflecting untreated growth, of which four preceded all treatment. Because tumours which are perceived to be growing are treated, the number of data points obtained is small and this is reflected in the fact that only eight growth slopes were significant at $p < 0.001$.

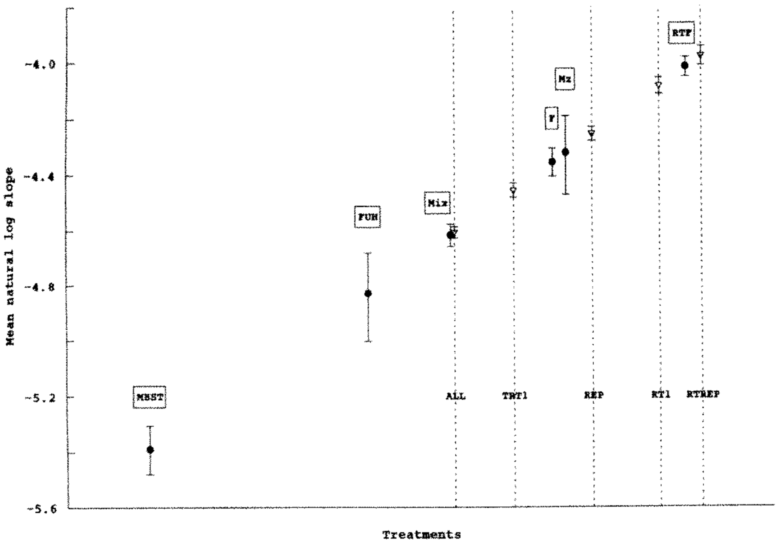

Figure 4. Mean natural log slopes, with 95% confidence limits, obtained in response to first treatments (boxed label, solid circle symbol). FUH = tamoxifen + fluorouracil; Mix = "mixture"; Mz = mitozantrone; RTF = radiotherapy first management. Other groupings (open inverted triangles, dotted lines): ALL = all negative slopes; TRT1 = all first treatments; REP = representative slopes; RT1 = all first (*e.g.* excludes biphasic second slope) radiotherapy slopes whatever timing; RTREP = representative slopes resulting from radiotherapy.

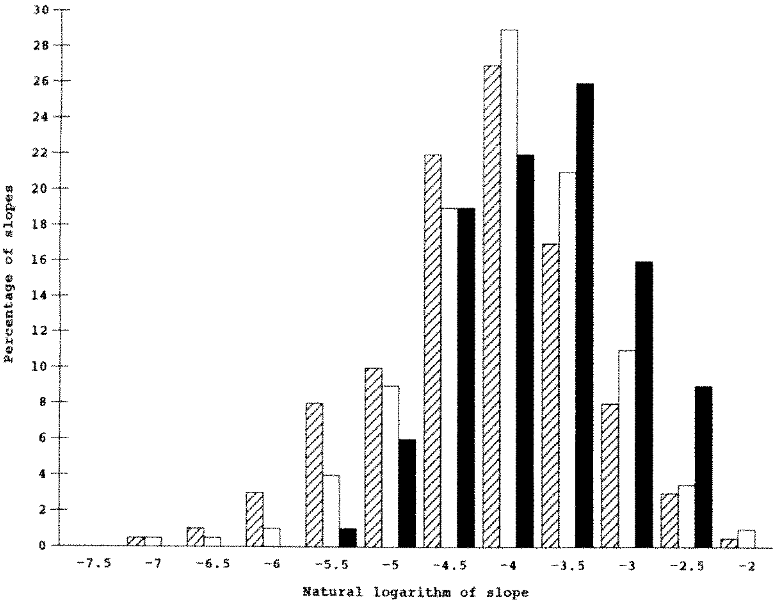

Figure 5. Distribution of resorption slopes (as natural logarithms of the unsigned slopes). Hatched bars = slopes resulting from first treatments, plain bars = representative slopes (steepest significant slope for each patient), solid bars = slopes resulting from radiotherapy as first management.

Resorption after radiotherapy

The delivery of drugs to a tumour site is problematical and the interplay of dose, cell-cycle timing and drug resistance is ill understood and unpredictable. In contrast, the energy of radiation *is* deposited in the defined field. We therefore restricted the investigation of the effect of dose, starting diameter, age and menopausal status upon resorption to slopes obtained from first radiation treatments where no previous management of any kind had occurred (68 patients).

The geometric mean resorption slope for this group of patients was the steepest (-0.0180, vht = 17 days). The range (-0.00392 to -0.0543, vht = 77 down to 5.5 days) was narrower than those of all representative and first treatment slopes with a higher percentage of slopes in the steeper groups (Fig. 5) but the distribution was still normal after natural log transformation. The mean age (58 years) was close to the overall mean (60 years) and the distribution of ages was also normal. The mean starting diameter of 56 mm was higher than in the full series (46 mm) owing to a relative paucity of tumours <30 mm in diameter (Table V).

We first inquired whether the radiation treatment schedule had affected the slopes. Within the dose range for radical radiotherapy, no correlation between the total dose and the slopes would be expected. Many of the tumours had disappeared before the full dose had been delivered: later fractions could therefore have no effect upon the steepness of the recorded slope. However, the number of fractions delivered and the time elapsed before the start of shrinkage varied considerably. In nearly half the cases shrinkage began with the first treatment, but for the greater part a range of 2–16 fractions was required and, in one extreme case, 21 fractions were delivered before the onset of resorption. The dose per fraction did not correlate with resorption slopes for the practical reason that gaps in treatment due to public holidays, machine breakdowns and transport problems meant that often the planned schedule was not achieved; for instance, a high dose per fraction might be combined with a protracted timing. The number of fractions required before shrinkage did show a correlation (-0.47, $p<0.001$) as did the time to shrinkage (-0.44, $p<0.001$). Because time and number of fractions is included in its time component, we concluded that the best measure of radiation delivered before the beginning of resorption would be the cumulative radiation effect (CRE) (Kirk et al, 1971). There was a negative correlation of CRE with slope, that is, large doses of radiation before shrinkage are associated with steeper slopes (Table VII). A small positive correlation between starting diameter and slope was seen, associating larger tumours with slower resorption.

We found no correlation between age and slope but there was a small positive correlation with menopausal status. This disagreement is explained by a considerable overlap of ages in the various menopausal groups. In descending order of steepness of the mean slopes were: 1, premenopausal; 2, postmenopausal; and 3, perimenopausal patients (Duncan's multiple range test). Although the mean postmenopausal slope was less steep than the

Table VI. Treatments associated with representative slopes

Radiotherapy	92
Hormone	8
Radiotherapy/hormone parallel	1
Radiotherapy/chemotherapy parallel	18
Chemotherapy	63
Chemotherapy/hormone parallel	56
Total	238

Table VII. Correlation between slopes and CRE, starting diameter and menopause Spearman coefficients

Factor	Coefficient	p
CRE before shrinkage	−0.47	0.0001
Mean diameter (mm)	0.29	0.018
Menopausal status	0.30	0.014

Table IX. Regression model

Factor	Estimate		p
Intercept	a	3.280	0.0001
CRE	b_1	−0.001	0.0001
Diameter	b_2	0.006	0.0002
Menopause	b_3	0.458	0.02

premenopausal. the full range was seen in postmenopausal patients (Table VIII).

In order to evaluate the relative importance of these correlations, we entered our data into the linear regression model provided in the General Linear Models (GLM) procedure of the SAS package of the type

$$y = a + b_1x_1 + b_2x_2 + b_3x_3 \ldots$$

where y = slope, a = intercept, x_1 = CRE, x_2 = starting diameter and x_3 = menopausal status. The estimated values for these factors are shown in Table IX and a selection of predictions made by using these values in the model in Table X. Note that since our treatment groups were not designed for this purpose, not all possible combinations are represented in our results. The most influential factor was menopausal status, but the CRE and starting diameter could change the slope dramatically when their values were high. Comparison of the natural log slopes with predictions made by the model showed that the 95% confidence limits for the prediction for the mean slopes did not differ from the fitted slopes by more than ±0.5 log.

Preliminary conclusions

It would appear that our original hypothesis that each tumour should display a characteristic slope irrespective of treatment is untenable, for we have demonstrated a range of mean resorption slopes according to first treatment. A clue to the explanation of the apparent variation of effectiveness of treatments may lie in the unexpected finding, in the case of radiotherapy, that the greater the CRE before shrinkage, the more likely it is that the ensuing slope will be steep. This would imply substantial regrowth between the early fractions, which, when extrapolated to chemotherapy with its more extended timing and wider measurement intervals, might lead to the missing of the true resorption trough in the interval between injections. Each point on the graph would then represent the net resorption after shrinkage followed by some regrowth. In Fig. 6 these concepts are illustrated by data from two patients who produced identical slopes resulting from radiotherapy (vht = 9 days). In the first case we see the delay in the start of shrinkage associated with less than optimal fractionation and a suggestion of a scalloped appearance of the points registering the mean volumes. After each gap in treatment there may be a levelling off of the curve before shrinkage is resumed. This might seem unimpressive evidence were it not that previous treatment with "the mixture" had produced, on two separate occasions earlier in the course, resorption slopes with a vht of 6 days (we cannot, of course, be certain that the tumour had not changed in the interval). The second case shows a tumour which apparently changed little as a result of combination chemotherapy at 3-weekly intervals and then shrank with a vht of 9 days when treatment was changed to radiotherapy. The nearly steady state during chemotherapy may be explained by regeneration occurring with a slightly longer doubling time than the "representative" vht of 9 days. We have seen this phenomenon in several cases (Thomlinson, 1987a). Therefore, in order to demonstrate the "true" or steepest possible resorption slope, treatment must be such that significant regrowth between separate doses (of whatever modality) is prevented. For the very rapidly growing tumours this goal may be unattainable in the face of severe concomitant toxicity to normal tissues.

Table VIII. Relationships between menopausal status and slopes

Number	Status	Mean	Range
13	Premenopausal	−0.0254	−0.00942 to −0.0531
45	Postmenopausal	−0.0177	−0.00600 to −0.0543
10	Perimenopausal	−0.0126	−0.00392 to −0.0352

Table X. Predictions from the model, menopausal status ranked 1, 2, 3 in order shown

Diam. (mm)	CRE	Premenopausal slope	Postmenopausal slope	Perimenopausal slope
30	200	−0.0243	−0.0154	−0.00972
	600	−0.0362	−0.0229	−0.0145
	1000	−0.0540	−0.0342	−0.0216
	1400	−0.0806	−0.0510	−0.0323
50	200	−0.0215	−0.0136	−0.00862
	600	−0.0324	−0.0207	−0.0132
	1000	−0.0483	−0.0308	−0.0196
	1400	−0.0715	−0.0452	−0.0286
80	200	−0.0180	−0.0114	−0.00700
	600	−0.0271	−0.0173	−0.0110
	1000	−0.0404	−0.0257	−0.0164
	1400	−0.0597	−0.0378	−0.0239

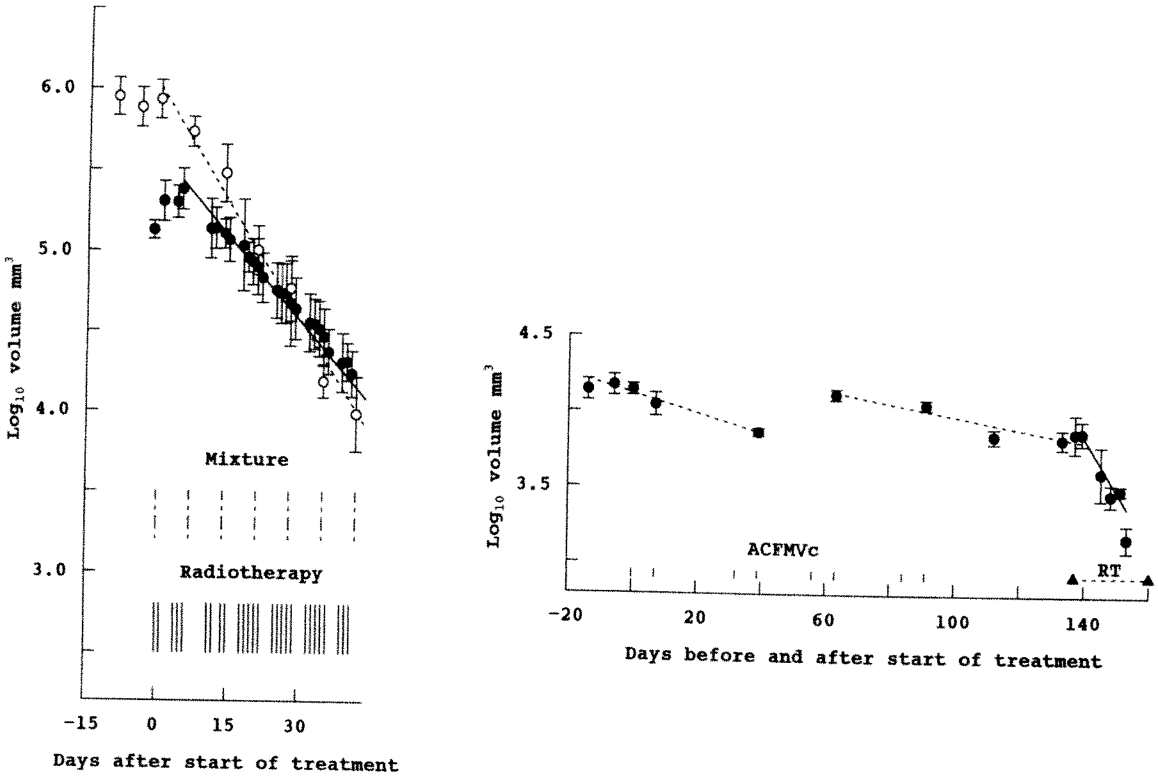

Figure 6. Data from two patients where chemotherapy preceded irradiation. The radiotherapy slopes are the same (−0.035, vht = 9.0 days; single line). In the first graph the slope attributable to "the mixture" (−0.0479, vht = 6.3 days; open symbols, dotted line) has been superimposed upon the radiotherapy one. The tumour had enlarged almost to the original size before it was irradiated. In the second case, ACFMVc = adriamycin, cyclophosphamide, fluorouracil, methotrexate and vincristine administered as ACFVc on Day 1 and ACMVc on Day 8 of a monthly cycle.

The mean diameter at presentation and the menopausal status have been shown to have some correlation with the slope.

The linear model incorporating the CRE, menopausal status and starting diameter, although very interesting, unfortunately does not afford practical clinical help because of its dependence upon the CRE which will not be defined until treatment has been given, a high proportion of which must then be counted as wasted.

Other factors influencing regression slopes

In support of our original hypothesis we did find parallel resorption slopes reflecting different treatments over the time course of 61 cases (Cheung & Johnson, 1991). Through insights from a number of seminal cases it became evident that not only did the structure of the tumour exert a profound influence upon the slope but also that the changes brought about by treatment may produce a residuum to receive the next treatment which is, effectively, a new tumour from which a different slope might be expected.

The first example, unrelated to the present series, was a man with a well differentiated chondrosarcoma of the scapula. It happened that a series of radiographs, in which the apparently benign bone tumour was visible, had been taken for unrelated reasons during the preceding 10 years. Planimetry measurements of the increasing area of the tumour enabled the construction of a growth slope (0.0161, doubling time = 19 months. Accurate volume estimations could not be made, but, assuming a spherical shape, the corresponding volume doubling time (vdt) would be 12.5 months). Figure 7 illustrates the effect of treatment by radiotherapy. A second biopsy 3 months after the end of treatment revealed no evidence of active tumour and the patient survived another 7 years without evidence of renewed growth. This result would have been registered as "no change" by the International Classification of Response (Hayward et al, 1977) and without our measurements further treatment by highly toxic chemotherapy might well have been given. The tiny volume of cell loss cannot be reflected in a resorption slope because the rigid cartilaginous framework remains and calcifies rather than resorbs after the death of the clonogenic cells.

Next came 22 patients who produced biphasic slopes in response to radiotherapy (Thomlinson, 1982), one example of which is shown in Fig. 8. (Note in passing that not only was there a sharp inflection between the

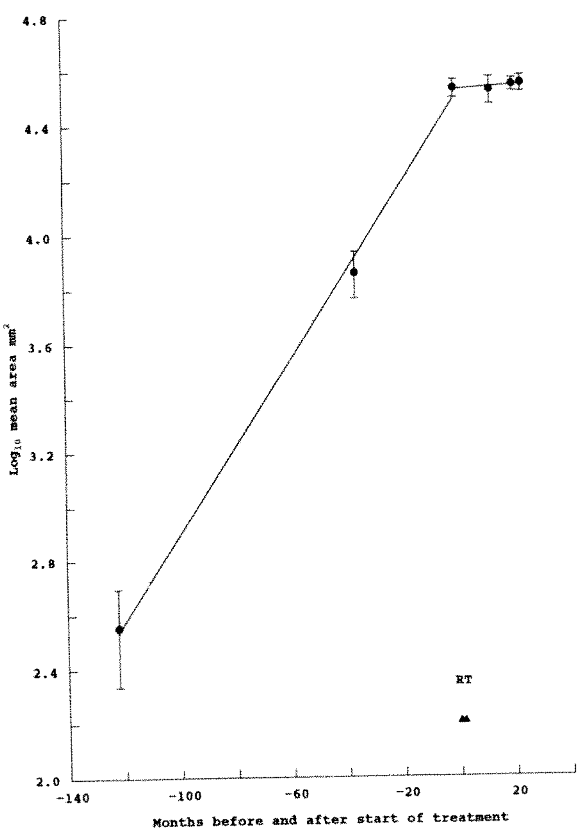

Figure 7. Ten years' recorded growth of a well differentiated chondrosarcoma and its response to irradiation.

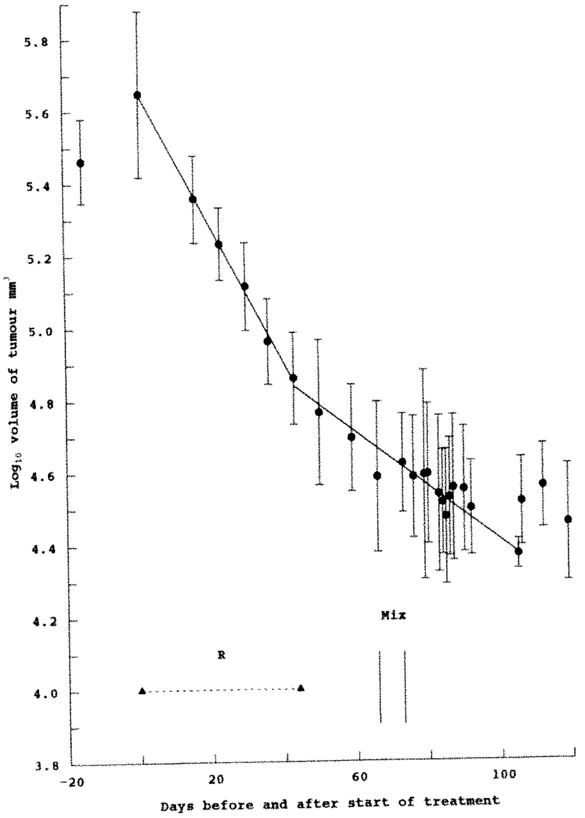

Figure 8. Example of biphasic resorption in response to radiotherapy. Starting diameter = 95 mm, diameter at point of inflection = 51 mm. 1st slope −0.0189, vht = 16 days, 2nd slope −0.00751, vht = 40 days.

earlier, steeper slope and the later, shallower one, but also that the addition of chemotherapy during its time course did not change the second slope.) Quantitative estimation by Dr R. H. Thomlinson of the relative proportions of collagen and parenchyma in a drill biopsy from another of these tumours confirmed that the steeper slope (vht = 49 days) corresponded with the removal of the small proportion of parenchyma (12%) and the flatter slope (vht = 185 days) with the high proportion of collagen (53%) in the outer rim of the tumour (Thomlinson, 1987b). Thus the change in steepness of resorption slope coincided with a major alteration in the composition of the tissue which was being removed.

Finally, in the case illustrated in Fig. 9, where treatment was by a standard combination chemotherapy regime until this was abandoned in favour of radiotherapy, six parallel resorption slopes have been fitted (vht = 30 days), together with a similar growth slope (vdt = 26 days). This case was reported by Thomlinson (1982). The explanation offered by him for the failure of every third treatment, whether by drugs or radiation, was that, while the first treatments were removing the cellular rim, sequestered cells lying in the core of the tumour would be protected by a poor circulation. Such cells near the periphery of the core would receive an improved blood supply after the early shrinkage and regrow the rim. If this situation could be clearly identified in prospect, the moment of exposure of the core should signal a change of management, whether to excision of the residue or modification of radiotherapy by the use of implantation, sensitizers, heavy particles, or perhaps, hyperthermia. (This particular tumour was inoperable and the metastases the major problem.)

Discussion

We must resist the temptation to treat resorption data as though the slopes were survival curves and the varying times to the start of shrinkage during radiation were shoulders or iso-effect points on such curves. The advances in the management of leukaemia in the 1960s derived directly from the plausibility of using cell counts as though they represented points on a survival curve and to schedule treatment accordingly (Skipper & Perry, 1970). Our chondrosarcoma is the extreme example of the reason why solid tumours are so disappointingly different: a lifetime cure for this patient resulted in no negative slopes. Since most breast cancers have a very

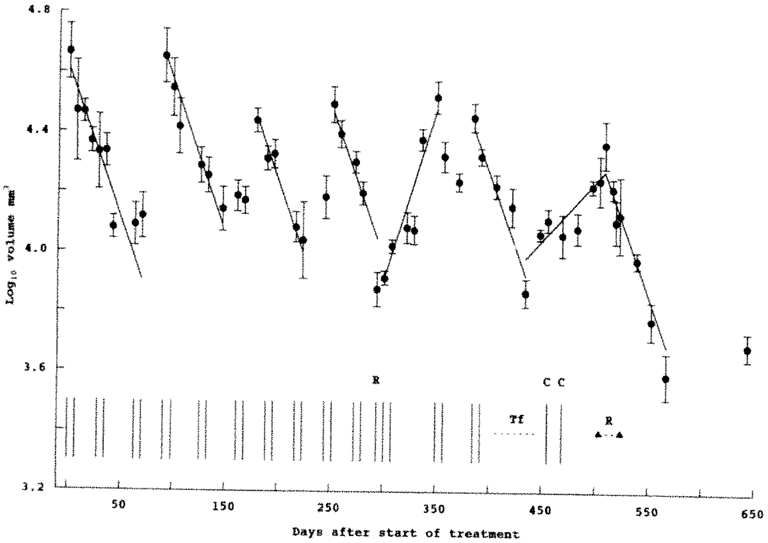

Figure 9. A puzzling relationship of chemotherapy timing and resorption slopes. All unlabelled vertical treatment lines represent courses of cyclophosphamide 400 mg, vincristine 1 mg, and doxorubicin 20 mg on Days 1 and 8 together with fluorouracil 500 mg on Day 1 or methotrexate 25 mg on Day 8 of a 28-day cycle. Single R = 1000 cGy one fraction. All the resorption slopes are parallel.

low growth fraction (in the range <1% to, rarely, more than 14%; Schiffer, 1978) removal of the volume of the proliferating cells will seldom be expressed separately in a resorption slope; assuming a growth fraction of 10%, the removal of these cells from a tumour 50 mm in diameter would reduce the diameter by only 1.8 mm.

After the death of the proliferating compartment the remainder of the tissue will die at a range commensurate with the natural life span of the other components which are not being replaced. The dead tissue may be removed but may also condense into a scar. The permutations of different components and growth rates mean that we may expect a wide range of resorption slopes to reflect the *same* clonogenic cell kill. Our findings suggest that the damage to proliferating cells must reach a level which precludes significant regrowth between radiation fractions or chemotherapy doses if the maximum possible resorption slope is to be recorded. This has been demonstrated for radiation by Trott et al (1987) in a mouse adenocarcinoma where a slower resorption slope resulted from lengthening of the fractionation interval to 48 hours. These remarks should not be taken to imply that the maximum resorption slope should always be pursued in the clinic; for instance, local control in the case of the elderly woman whose data is shown in Fig. 2 was achieved without toxicity. However, resorption slopes in isolation should not be used in extrapolations about the growth behaviour of human tumours because of the uncertainty whether the maximum steepness of slope has been seen. This contrasts with the controlled, experimental situation, where the use of transplants of the *same* tumour establishes the definitive resorption slope (Thomlinson & Craddock, 1967). The effectiveness of different treatments may then be evaluated without confusion by potentially different intrinsic growth rates.

Whatever the interpretation of the slopes, the effect of radiotherapy or chemotherapy is the consequence of the death of clonogenic cells. The introduction of hormone therapy adds a different dimension, for hormones are messengers: "don't proliferate" may delay the progress of a tumour possessing the right receptors but does not result in clonogenic cell death. Once proliferation has ceased, death of the non-proliferative cells through natural attrition will produce useful shrinkage. In due course, treatment by hormones alone will lead to renewed growth. In order to respond to messages, a degree of differentiation is required which betokens slower growth. This may explain the shallow mean resorption slope for hormone-associated treatment. We cannot claim that no steep slopes exist, since our interpretation of the function of hormones and the fact that only about one third of tumours are known to be hormone-controlled precluded their use as first management in our practice.

In individual cases a different resorption slope may be seen in response to subsequent treatments or at a later stage in the same treatment. Without histological evidence we cannot distinguish between a shallower subsequent slope which results from a poorer treatment and that which is the result of a change in the tumour composition brought about by the earlier treatment (Fig. 8). "Cross-over" testing of drug regimes is seen to be meaningless unless a new biopsy is performed just before the alteration of treatment. The shallower mean slopes associated with MBST alone result because this style of management *works* for tumours which change relatively slowly. Those which changed rapidly either produced steeper slopes with the first single agent without responding to hormones, or the tumour failed to shrink so that treatment was changed to combination chemotherapy ("the mixture"), radiation or surgery.

We have defined a "representative" slope for each tumour as the steepest significant one. Since most later patients received neither intensive chemotherapy nor radiation to the intact tumour, we cannot be sure that the maximum possible resorption rates were seen; in our clinical management it was enough that the tumour was shrinking steadily. The slow tail in the distribution of representative slopes suggests that, indeed, in some cases the maximum was not reached.

No information about the growth rate was available at the time of treatment planning for the tumours treated by radiotherapy first, so that patients with rapidly growing tumours could not be selected to start treatment on Mondays; as few as one or two fractions might be given before a long weekend. In such cases a large part of the early treatment may have been wasted in starting resorption, implying a lost opportunity for reoxygenation and an increasing probability of failure to control the tumour. By the time that patients who received MBST as the first management required irradiation the resorption data and histology were known; extra efforts were then made to ensure prompt treatment and to foresee problems for fractionation in those cases known to have rapid growth rates. Our preliminary results (unpublished) suggest that the local control rate has been improved.

It is not surprising that some relationship between starting size and slope has been found. Patients generally perceive change and may therefore report more rapidly growing tumours sooner. On the other hand, procrastination may occur more often with slowly growing lumps where changes from week to week are small. These latter patients present when the integrity of the overlying skin is threatened. The very large tumours are probably in a separate category where mechanical factors are more important than the intrinsic properties of the cancer. The failing circulation, leading to gross hypoxia, will protect from radiation or drug mediated damage and the steepness of the resorption slope may be modified in an unpredictable manner by the reduced rate of removal of dead tissue. This has very important implications for rigid radiation schemes where up to half the total dose may be given to the unchanged, and therefore hypoxic, tumour.

The correlation of young, premenopausal patients with steep slopes accords with general experience that younger women have more rapidly growing tumours and a poor prognosis in that their metastases show up sooner than for more slowly growing ones (Kusama et al, 1972). The converse is *emphatically* not so: postmenopausal and elderly patients experience the full gamut of resorption slopes and growth rates. The practice of giving all elderly women a palliative hormone treatment and reviewing some months later can only lead to some tragically uncontrollable local disease. The finding of shallower mean slopes in perimenopausal patients cannot be regarded as definitive owing to the small size of the group, the subjective evaluation of menopausal status and a skew distribution of these patients among the radiation fractionation schemes. These observations invite repetition with more patients upon whom hormone assays to determine the precise menopausal situation should be performed. Cell flow cytometry techniques also hold promise of identifying breast tumours with high potential doubling times (McDivitt et al, 1986; Remvikos et al, 1988).

Conclusion

We find that our original hypothesis that each tumour should produce a characteristic regression slope in response to treatment must be modified. In addition to the intrinsic range of resorption slopes inherent in the enormous variety of breast cancers, we have found variability of the effectiveness of treatment to confuse the evaluation of the individual case. Effective treatment, in this context, will be that which does not permit tumour regrowth between fractions, in the case of radiation, or doses, in the case of drug therapy. For the useful interpretation of regression slopes more information about the structure of the tumour and the relative proportions of different components is required. A report upon the quantitative histology of this series of tumours will be the subject of a later paper.

Acknowledgments

This is the second of a series of papers in which the work of a team led by the late Dr R. H. Thomlinson is presented. It was started under the auspices of the Medical Research Council of which he was a member of the External Scientific Staff until his retirement in 1987. Since 1986 the work has been financed entirely through the fund raising efforts of the Mount Vernon Breast Cancer Clinic Appeal (Chairman: Mrs J. Birdsall; Treasurer: Mr John Smith).

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Fractionated high dose rate *versus* low dose rate regimens for intracavitary brachytherapy of the cervix

I. General considerations based on radiobiology

By D. J. Brenner, PhD and E. J. Hall, DPhil

Center for Radiological Research, College of Physicians and Surgeons of Columbia University, 630 West 168th Street, New York, NY 10032, USA

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Abstract. Intracavitary brachytherapy at low dose rate (LDR), often with the addition of external-beam radiotherapy, has long been considered the treatment of choice for carcinoma of the cervix, maximizing acute damage in the treatment volume, whilst minimizing late effects. In recent years, primarily for reasons of convenience and cost, there has been a move towards treatments involving a few fractions at high dose rate (HDR). Using data from cells of human origin cultured *in vitro*, we make estimates of the doses that, delivered in 2–12 HDR fractions, produce tumour control and early effects equivalent to intracavitary treatments at LDR. We also show that, for situations where the normal-tissue dose responsible for late effects is significantly smaller than the tumour dose, HDR schemes may be devised which, while yielding early killing comparable with that of LDR, should not result in worse late effects. We suggest that this scenario probably applies to treatment of carcinoma of the cervix.

Intracavitary brachytherapy at low dose rate (LDR), often in conjunction with external-beam radiotherapy, has, for over half a century, been the treatment of choice for carcinoma of the cervix. Initially, radium tubes were used, supplanted in more recent years by caesium 137 or iridium 192 sources. A typical LDR regimen for cervical cancer involves two insertions, 1–3 weeks apart, to a total dose to point A of 40–60 Gy (plus an external whole-pelvic irradiation), or to a total of 75–80 Gy with no external treatment (Moss & Cox, 1989; Brenner & Hall, 1990). The LDR treatment is usually delivered at 0.5–0.7 Gy/h. Such lengthy irradiations, totalling 5–6 days, are based largely on historical precedent but, in retrospect, may be justified by the rationale that LDR schedules differentially spare late-responding tissues compared with early-responding normal tissue and tumour cells (Withers et al, 1982).

High dose rate (HDR) treatment for cervical carcinoma was introduced about 25 years ago, motivated by practical advantages to the patient who may avoid extensive confinement in bed and can usually undergo outpatient therapy. The reduction in radiation dose to nursing personnel is an additional advantage. A number of different HDR fraction numbers, from 2 to 15, are currently under consideration. From the treatment standpoint, HDR units provide accurate and flexible dosimetry, as well as increased patient throughput. The practical advantages of HDR have been summarized by Joslin (1989), but it is usually assumed that HDR represents a compromise between patient convenience and optimal therapeutic advantage.

In this work we use radiobiological data obtained with cells of human origin cultured *in vitro* to determine the doses which, delivered in a few fractions at higher dose rates, would yield results equivalent to LDR for tumour control and early effects. We also invoke basic radiobiological considerations to show that, when the dose-limiting normal tissues at risk for serious late effects receive a significantly lower dose than the tumour, a regime consisting of a few large fractions at HDR does not necessarily result in late effects worse than those of LDR. We suggest that treatment of carcinoma of the cervix by intracavitary brachytherapy may be such a case.

Methods

We use the linear-quadratic formalism as described by Lea and Catcheside (1942) and recently reviewed by Fowler (1989). The survival, S, at a dose D is written as

$$S(D) = \exp(-\alpha D - G\beta D^2) \qquad (1)$$

Equation (1) is derived from radiobiological considerations indicating that cell killing results from the interaction of pairs of elementary damaged species—probably DNA double-strand breaks—to produce an exchange-type chromosomal aberration which can cause lethality. The two terms in Equation (1) reflect the fact that the two elementary damaged species may be produced by the passage of the same track of radiation (linear term in dose) or by two independent radiation tracks (quadratic term).

If some time elapses between the passage of the first and second tracks, the first damaged site may be repaired before interacting with the second. This repair will result in a reduction in the second, quadratic term in Equation (1) by a factor denoted G by Lea and Catcheside (1942). This factor will depend on the time dependence of the repair of the elementary damaged species which, assuming exponential repair, can be described by one or more half-times for repair, τ. In addition G will depend on the nature of the temporal distribution of the dose. Formulae for G for various temporal irradiation schemes have been reviewed by Nilsson et al (1990) and Brenner and Hall (1991). The particular formula that will be used here is for the case of N equal fractions each of duration c and period b between fractions:

$$G = \frac{2t_0}{(Nc)^2}\left\{Nc + Nt_0\left(1 - \frac{1}{x}\right) + t_0\left(x + \frac{1}{x} - 2\right)\right. \\ \left. \times\left[\frac{N}{1-y} - \frac{y(1-y^N)}{(1-y)^2}\right]\right\} \quad (2)$$

where $x = \exp(-c/t_0)$, $y = \exp(-b/t_0)$ and $t_0 = \tau/0.693$.

In this section we seek HDR fractionation schemes that are equivalent to LDR treatments for intracavitary brachytherapy, in terms of tumour control and other early effects.

For tumour control and early normal-tissue effects (hereafter subscripted E) we assume that D_{CA} is the prescribed continuous LDR treatment total dose to the tumour, and wish to find the corresponding tumour dose (D_{FA}) that would give the same cell killing for a HDR fractionated regime. Thus from Equation (1)

$$\exp(-\alpha_{\mathrm{E}}D_{\mathrm{CA}} - G_{\mathrm{CE}}\beta_{\mathrm{E}}D_{\mathrm{CA}}^2) \\ = \exp(-\alpha_{\mathrm{E}}D_{\mathrm{FA}} - G_{\mathrm{FE}}\beta_{\mathrm{E}}D_{\mathrm{FA}}^2) \quad (3)$$

where α_{E} and β_{E} are the appropriate parameters in Equation (1) for early effects. G_{CE} and G_{FE} are calculated from Equation (2) for appropriate values of the fraction time (c), period between fractions (b), fraction number, and half-time for repair of early effects (τ). Here, and throughout the paper, we assume that the LDR and HDR regimes have the same total duration so that, to a first approximation, cell proliferation would be the same in both cases.

Equation (3) can be written

$$\left(\frac{\alpha}{\beta}\right)_{\mathrm{E}} = \frac{G_{\mathrm{FE}}D_{\mathrm{FA}}^2 - G_{\mathrm{CE}}D_{\mathrm{CA}}^2}{D_{\mathrm{CA}} - D_{\mathrm{FA}}} \quad (4)$$

and the solution for D_{FA} is

$$D_{\mathrm{FA}} = \frac{1}{2G_{\mathrm{FE}}} \\ \times\left\{\sqrt{4G_{\mathrm{FE}}D_{\mathrm{CA}}\left[\left(\frac{\alpha}{\beta}\right)_{\mathrm{E}} + G_{\mathrm{CE}}D_{\mathrm{CA}}\right] + \left(\frac{\alpha}{\beta}\right)_{\mathrm{E}}^2} \right. \\ \left. - \left(\frac{\alpha}{\beta}\right)_{\mathrm{E}}\right\} \quad (5)$$

Thus, knowing G_{FE} and G_{CE} (see Equation (2)) as well as $(\alpha/\beta)_{\mathrm{E}}$, the equivalent HDR tumour dose, D_{FA}, can be estimated. In the next section we shall discuss appropriate values for the parameters $(\alpha/\beta)_{\mathrm{E}}$ and τ_{E}, and then estimate equivalent (for early effects) HDR doses for a variety of practical situations.

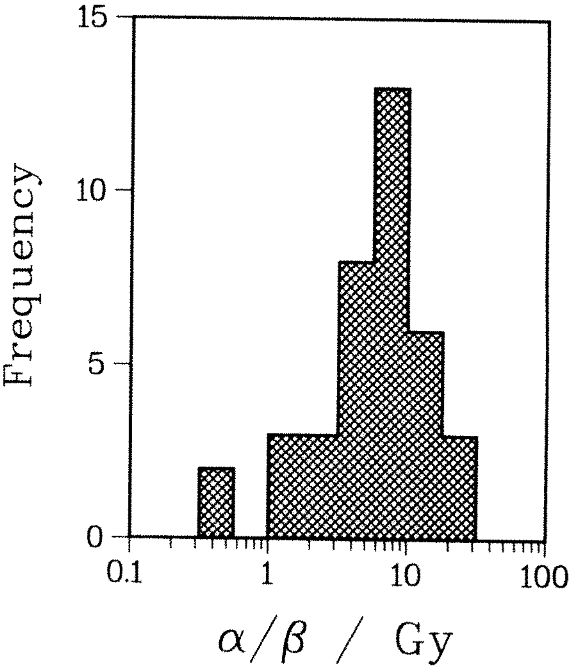

Figure 1. Distribution of 38 values of α/β, taken from analysis of *in vitro* LDR studies on 38 cell lines, both normal and malignant, of human origin (see Brenner & Hall, 1991).

Estimation of HDR doses to produce tumour control and early effects equivalent to those of LDR

We can now use Equation (5) with parameters $[(\alpha/\beta)_{\mathrm{E}}, \tau_{\mathrm{E}}]$ to calculate the total dose, D_{FA}, in the HDR fractionated scheme, that would give early effects equivalent to those of the LDR treatment. We first discuss the generation of appropriate parameters.

The recent availability of many *in vitro* LDR survival curves for cells of human origin allows increased precision (relative to that available from analysis of *in vivo* data) with which survival parameters can be estimated from *in vitro* data. The generation of these parameters from LDR survival curves is described by Brenner and Hall (1991). The data are for a mixture of normal and malignant human cell lines. In that the cells are cycling, and have α/β ratios comparable with those obtained from *in vivo* data for early effects, we assume that this information is a good data base for predicting early response to radiation *in vivo*. A major part of this paper involves testing this assumption. Figures 1 and 2 show distributions of $(\alpha/\beta)_{\mathrm{E}}$ and τ_{E}, derived from analyses of experiments with 38 cell lines of human origin. No single value of a given parameter is descriptive of the variety of cells evaluated—or, presumably, of a realistic *in vivo* situation.

For a given HDR fractionation scheme, we may now calculate the HDR point-A dose which will be equivalent to an LDR schedule. For each of the 38 parameter sets summarized in Figs. 1 and 2, we use Equation (5) to calculate a total HDR dose that will give an early effect

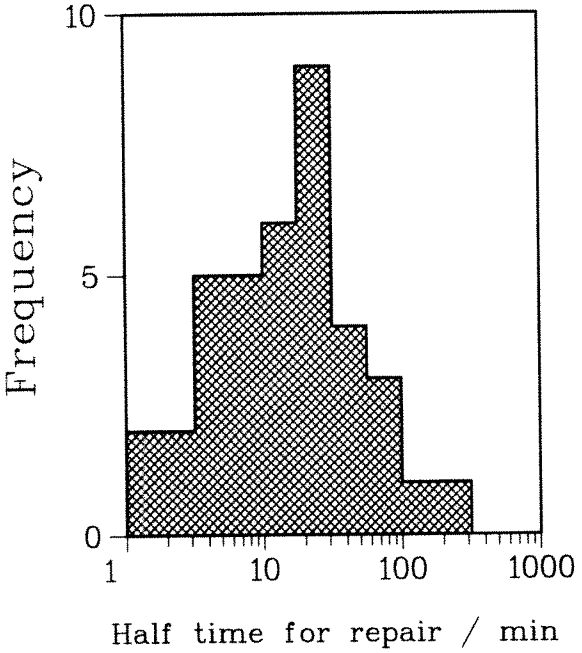

Figure 2. Distribution of 38 values of the half-time for sublethal damage repair, taken from analysis of *in vitro* LDR studies on 38 cell lines, both normal and malignant, of human origin (see Brenner & Hall, 1991).

equivalent to that of LDR. The result will be a distribution of 38 doses, one for each parameter set.

Test of technique for matching early effects using known clinical data

As a first check on this approach, we show in Fig. 3 the distribution of total point-A doses delivered in two fractions at 1.6 Gy/h which are predicted (based on the range of parameters shown in Figs. 1 and 2) to give the same acute effects as two weekly fractions totalling 75 Gy, at 0.53 Gy/h. This calculation relates to a Christie Hospital clinical trial (Stout & Hunter, 1989) to establish an equivalent dose when the dose rate is increased from 0.53 to 1.6 Gy/h. No external radiotherapy was used in the trial. Stout and Hunter (1989) concluded that acceptably equivalent doses to 75 Gy at 0.53 Gy/h ranged from 62 to 68 Gy at 1.6 Gy/h. The mean of the distribution in Fig. 3 is 64 Gy (SD 12 Gy), in good agreement with that found clinically. Thus our approach appears to have predictive value, at least in terms of acute effects.

The 15% dose reduction suggested here in moving from 0.53 Gy/h to 1.6 Gy/h is in contrast to the 25% reduction adopted by the Glasgow group (Symonds et al, 1989), based on the CRE formula (Kirk et al, 1972). As might be expected based on the considerations discussed here, in clinical trials the Glasgow group reported that their higher dose rate arm showed a trend towards decreased tumour control and patient survival compared with LDR (Symonds et al, 1989).

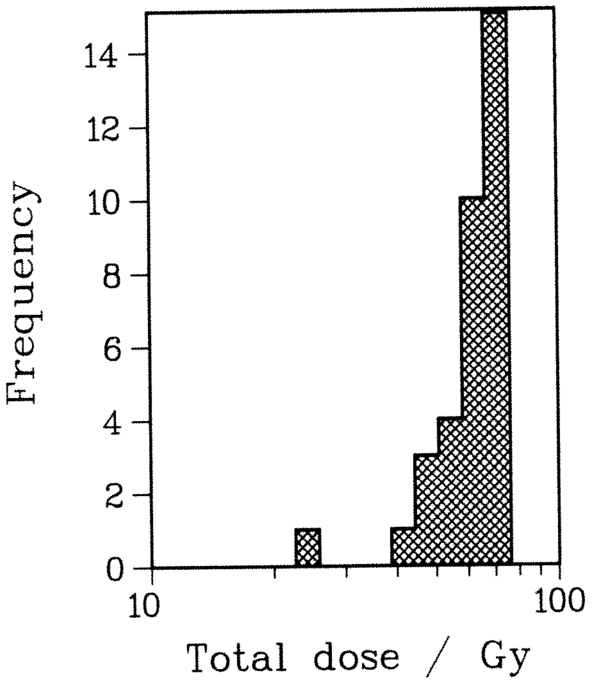

Figure 3. Distribution of total prescribed treatment doses delivered in two fractions at 1.6 Gy/h that are predicted (based on the 38 parameter sets of Figs. 1 and 2) to give the same acute effects as two weekly fractions totalling 75 Gy, at 0.53 Gy/h. The arithmetic and geometric means are, respectively, 64 Gy and 62 Gy, which may be compared with the clinically determined equivalent dose (Stout & Hunter, 1989) of 62–68 Gy.

Use of technique for matching early effects at HDR to those at LDR

The same approach can be used to calculate HDR dose schemes equivalent to conventional LDR schemes. We first calculate HDR treatments equivalent (for early effects) to an LDR schedule of 75 Gy delivered in two weekly fractions at 0.53 Gy/h. This is a typical LDR regime for those situations where external teletherapy is not used (Stout & Hunter, 1989). Figure 4 shows, for different numbers of HDR fractions, the distribution of HDR doses predicted (based on the 38 parameter sets summarized in Figs. 1 and 2) to yield acute effects equivalent to 75 Gy at 0.53 Gy/h. Each HDR fraction is assumed to take 450 s (though the precise time is not critical to the results), and the total treatment time is held at 10 days, to minimize the relative importance of cellular proliferation. The variation with fraction number of the mean dose per fraction, derived from such calculations, is shown in Fig. 5.

The calculations reported above have been for brachytherapy alone, *i.e.* without an external whole-pelvic boost. In such whole-pelvic external irradiations, the critical organs will receive a larger proportion of the total tumour dose. As a guide to the design of such mixed-modality regimens involving brachytherapy and external radiation, Fig. 6 shows, for various HDR frac-

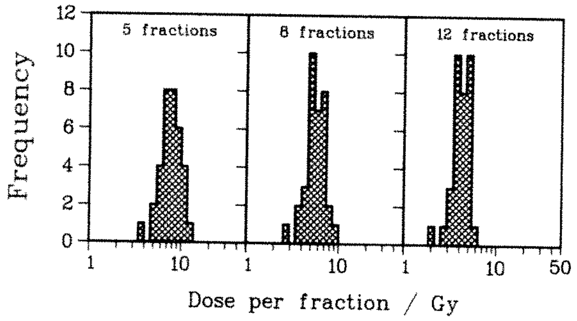

Figure 4. Distributions of doses for 5, 8 and 12 fractions at HDR predicted (based on the 38 parameter sets summarized in Figs. 1 and 2) to yield equivalent acute effects to 75 Gy at 0.53 Gy/h, delivered in two weekly fractions. Each HDR fraction was assumed to take 450 s, and the total treatment time was 10 days.

tion numbers, the mean point-A HDR doses predicted (based on the 38 parameter sets of Figs. 1 and 2) to yield acute effects comparable with two fractions totalling 60 Gy, delivered at 0.5 Gy/h. This latter is a typical LDR brachytherapy regime used in conjunction with external whole-pelvic irradiation. Figure 6 also shows a comparison with the regimens reported in the literature as having been used for such HDR clinical trials. There is reasonable agreement between the dose regimens predicted from radiobiological considerations and those derived from clinical experience for the HDR protocols. Further comparisons with a variety of practically used LDR schemes (including the effects of whole-pelvic irradiation) are presented elsewhere (Brenner & Hall, 1990).

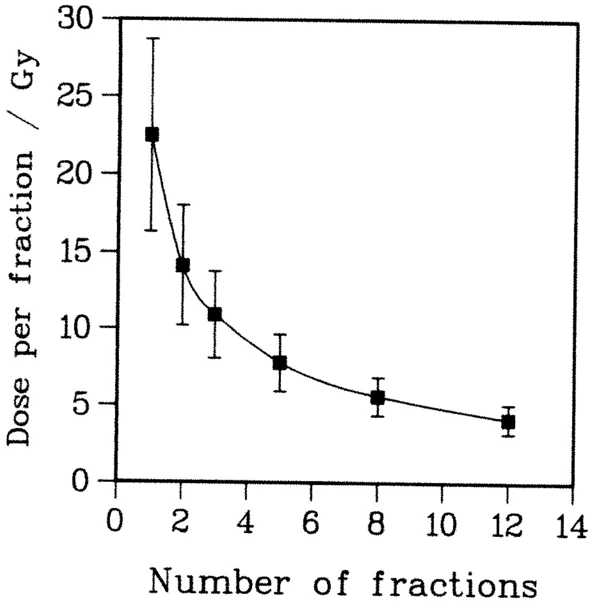

Figure 5. Arithmetic means of the distributions shown in Fig. 4. The bars correspond to the standard errors of the samples in Fig. 4. Also included are data for one, two and three fractions.

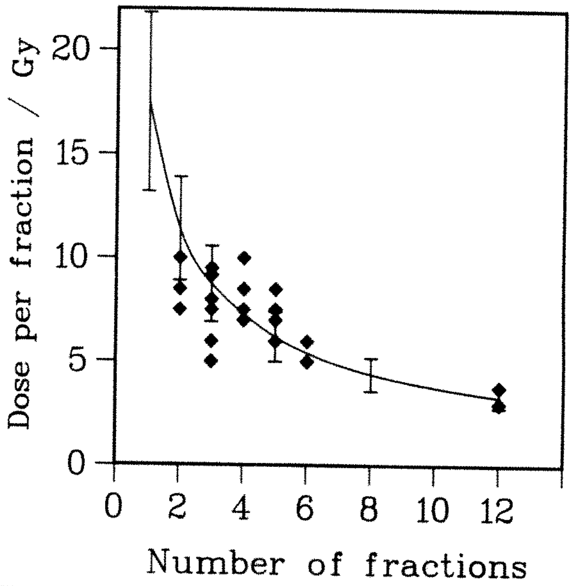

Figure 6. Mean point-A HDR doses predicted (based on the 38 parameter sets of Figs. 1 and 2) to yield acute effects comparable with two fractions totalling 60 Gy, delivered at 0.5 Gy/h. In each case the total treatment time was 23 days. The bars correspond to the standard error of the means of the results calculated using the 38 data sets described in the text. The points represent HDR intracavitary brachytherapy regimens reported in the literature to have been used in clinical trials.

Late effects

The appreciation that early-responding and late-responding tissues differ in their response to fractionation is probably the most important advance in radiation therapy in the last decade. *In vitro* data are consistent with the notion that late-responding tissues have α/β ratios that are usually significantly smaller than those corresponding to early-responding normal tissues and tumours. This idea was first proposed by Withers and his colleagues (*e.g.* Withers et al, 1982) and has since been widely used (*e.g.* Fowler, 1989). The practical outcome of the different shapes of dose–response relations for early and late effects is that late-responding tissues are more sensitive to changes in fractionation patterns than early-responding tissues. Consequently, when matching a protocol consisting of a few large fractions to one involving many small fractions (or continuous LDR), if the doses are adjusted (as, for example, in the last section) to result in equivalent early effects, then the risk of late effects will be greater for the protocol involving the few large fractions. This conclusion follows from laboratory studies (*e.g.* Withers et al, 1978) and has been unequivocally demonstrated in the clinic (*e.g.* Bates & Peters, 1975).

The notion that for matched early effects, late effects will be worse for an HDR protocol, is in general true if the normal tissues at risk for late effects receive about the same total dose as the early-responding tissues for which the doses were matched. This is the situation that generally holds in external beam therapy. However, we shall show that it is not necessarily true if the late-responding tissues at risk receive a dose *lower* than the prescribed treatment dose. This will be formulated mathematically under the usual assumption that late effects are related to survival of clonogenic cells that could avert a late response (Hendry & Thames, 1986).

We assume that we have already estimated the prescribed HDR dose (D_{FA}) to produce early effects in the treatment volume equal to those produced by a dose D_{CA} at LDR (using the techniques described above). Now we are interested in finding if there is a point, at some distance from the treatment volume, where there would be *equal* survival at HDR and LDR of the cells responsible for averting a *late* response. We assume that the dose to the normal tissue at this point is a factor R smaller than the prescribed dose to the treatment volume. The doses to this point will then be $R \times D_{FA}$ at HDR or $R \times D_{CA}$ at LDR. Thus for equal survival at HDR to LDR at this point, analogously to Equation (3),

$$\exp(-\alpha_L R D_{CA} - G_{CL}\beta_L R^2 D_{CA}^2) = \exp(-\alpha_L R D_{FA} - G_{FL}\beta_L R^2 D_{FA}^2) \quad (6)$$

where the subscript L refers to late effects. Equation (6) has a solution, so there is a point, at some distance from the treatment volume where, for matched early effects in the treatment volume, the late effects at that point would be the same for HDR as for LDR. The dose at that point is smaller than that in the treatment volume by the factor R, the solution to Equation (6):

$$R = \left(\frac{\alpha}{\beta}\right)_L \frac{D_{CA} - D_{FA}}{G_{FL} D_{FA}^2 - G_{CL} D_{CA}^2} \quad (7)$$

where D_{FA} is the HDR tumour dose giving acute effects equivalent to those of D_{CA} at LDR (see last section). So, assuming that the LDR and HDR tumour doses have been matched to give equal acute effects, if the critical normal tissue responsible for late effects received a dose $R \times D_{CA}$ at LDR (or $R \times D_{FA}$ at HDR), late effects would be the same for the LDR and HDR regimes. On the other hand, if the critical normal tissue were closer to the tumour and received a dose greater than $R \times D_{CA}$ at LDR (or greater than $R \times D_{FA}$ at HDR) then there would be more late effects in the HDR treatment. Conversely, if the critical normal tissue were further from the tumour and received a dose less than $R \times D_{CA}$ at LDR (or $R \times D_{FA}$ at HDR) then the HDR treatment would result in *less* late effects than LDR.

Thus as one moves further away from the tumour, *i.e.* as the dose to normal tissue becomes a smaller fraction of the tumour dose, the notion that, for matched early effects, HDR will always produce more late effects than LDR becomes less valid, until a point is reached (given in terms of dose reduction by Equation (7)) when the late effects are equal. Moving even further away from the tumour will then result in less late effects for HDR than for LDR.

This principle can be illustrated with the following approximation: if the repair rates were the same for early and late effects, then $G_{CE} = G_{CL}$ and $G_{FE} = G_{FL}$, and by reference to Equation (4)

$$R = \frac{(\alpha/\beta)_L}{(\alpha/\beta)_E} \quad (8)$$

This simple result says the following: when the dose of an HDR regime is matched to produce early effects equal to those of an LDR regime, if the dose responsible for late effects is less than the tumour dose by a factor more than the ratio of α/β for late effects to α/β for early effects, then the HDR late effects will not be worse than those at LDR.

Let us assume "typical" α/β ratios of 4 Gy for late effects (Turesson & Thames, 1989) and 8 Gy for early effects (Brenner & Hall, 1991); then in the approximation that repair rates are the same for early and late effects, Equation (8) implies that if the dose to the tissue responsible for late effects were about half that of the tumour dose, HDR would produce late effects similar to those of LDR—assuming the full tumour doses at HDR and LDR were matched for equal early effects.

An extreme case occurs if τ_L is very long so that there is little repair of late damage. Now if the LDR and HDR tumour doses are matched for equal acute effects, then the late effects from HDR will be less in *all* positions than LDR late effects—because the late effects will depend only on the total dose at any point, which will always be less for HDR. This situation was pointed out by Orton (1987), though such a complete absence of repair for late effects seems unlikely.

The ideas and conclusions reached in the above calculations are illustrated in Fig. 7. The upper panel shows typical dose–response curves for late effects from LDR and HDR (based on the parameters given in the caption). The prescribed tumour doses (matched for equal early effects as in the previous section) are 75 (LDR) and 22.5 Gy (HDR). The lower panel in Fig. 7 shows portions of the same dose–response curves, but plotted as function of the relative dose as we move away from the point at which the full dose is prescribed. At the point where the full dose is prescribed the LDR regimen yields a greater survival, and therefore a smaller risk of late effects. However, because the HDR dose–response relation is more curved than that for LDR, reducing the HDR dose by a given fraction will have a much greater sparing effect than reducing the LDR dose by the same fraction. Thus at some distance from the point where the full dose is prescribed, where the dose is less than the prescribed dose by a factor R (see Equations (7)–(9)), the curves will cross and HDR will produce late effects equal to those of LDR. In the case shown in Fig. 7, R is about 0.8, and so if the normal-tissue dose responsible for late effects is less than 80% of the prescribed tumour dose, the HDR regime will yield greater survival, and therefore less late effects. If, for example, the dose to the

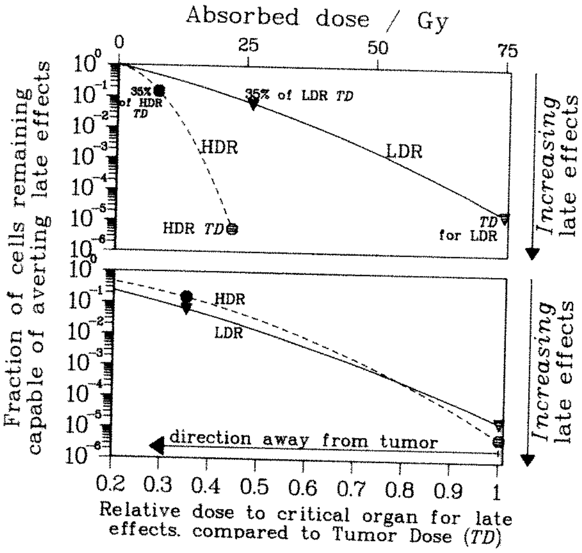

Figure 7. Top panel. *Full curve* is predicted survival for cells responsible for late effects for an LDR regimen of two weekly 3-day fractions. The LDR tumour dose (TD) is 75 Gy at 0.53 Gy/h. Smaller doses correspond to points distal to the treatment volume, which thus receive dose at a comparably lower dose rate. *Dashed curve* is the same for a single-fraction HDR treatment, for a tumour dose of 22.5 Gy chosen, as described earlier in the text, to match the *early* LDR effects. **Bottom panel.** Same curves as top panel, but plotted as the dose *relative* to the tumour dose. Three cases can be identified. (a) At the tumour (right side of bottom panel) the critical normal tissue dose is the same as the tumour dose; in this case the late effects will be worse (*i.e.* less survival) for HDR compared with LDR. (b) The critical normal tissue dose is ~0.8 of the tumour dose; in this case HDR and LDR will produce about the same late effects. (c) The critical normal tissue dose is much less (*e.g.* 35%, illustrated here) than the tumour dose; in this case HDR will produce less late effects (greater survival) than LDR. Parameters used in the calculation were, for early effects, $\alpha_E = 0.36\ \text{Gy}^{-1}$, $\beta_E = 0.068\ \text{Gy}^{-2}$, and $\tau_E = 32$ min; for late effects, $\alpha_L = 0.084\ \text{Gy}^{-1}$, $\beta_L = 0.021\ \text{Gy}^{-2}$, and $\tau_L = 23$ and 252 min (two equally effective repair processes).

critical normal tissues were only $0.35D_A$ (as shown in Fig. 7), the HDR regime, for matched early effects, would yield a smaller risk of late effects than LDR.

So far, the rather novel radiobiological principle discussed here—a special case of which was pointed out by Orton (1987), and further developed by Dale (1990)—though of theoretical interest, is of uncertain practical application. Next, we draw on the currently available clinical and dosimetric experience with cervical brachytherapy to investigate whether this principle is relevant to the development of late effects after HDR brachytherapy of cervical carcinoma.

Calculation of late-effect probabilities

To calculate the absolute probability, P, of late effects, we use a Poisson model (Gilbert, 1974; Hendry, 1989):

$$P = \exp\{-\exp[\ln(K) - \alpha D_N - G_L \beta_L D_N^2]\} \qquad (9)$$

Here, D_N is the dose to the normal tissue that is responsible for the late effects and is given by

$$D_N = rD_A \qquad (10)$$

where D_A is the prescribed treatment dose (calculated, for HDR, by matching early effects to LDR, as described earlier) and r is the factor by which the critical normal tissue dose is less than this prescribed dose (we term this latter the critical normal-tissue dose reduction). The parameter K represents the effective number of "tissue rescuing units" (Hendry & Thames, 1986), and α_L, β_L and G_L are the counterparts to α_E, β_E and G_E, but referring to cells in late-responding rather than early-responding tissues.

Thus, in order to make quantitative predictions of late-effect probabilities, we need a value for the quantity r, the factor by which the critical normal tissue dose for late effects is smaller than the prescribed dose.

In the case of the treatment of carcinoma of the cervix by intracavitary radiotherapy, the normal tissues that are close to the radioactive sources, such as the vaginal mucosa, are highly resistant to radiation, while the late-reacting tissues that are dose limiting, such as the rectum and bladder, are usually more distant from the radioactive sources. Thus the dose to normal tissue that may cause a dose-limiting late reaction is likely to be smaller than the point-A dose (*i.e.* r, the critical normal-tissue dose reduction, is less than one). Some typical doses (relative to point A) to normal-tissue organs which may give a late response are shown in Table I. For the rectum, which is the site of the majority of late effects after brachytherapy of the cervix, the average doses relative to point A vary from ~60% at the anterior surface to about 30% at the posterior wall.

The significant variation in dose across both the rectum and bladder make it impossible to specify, *a priori*, what dose should be used when estimating late effects. It is tempting to use the maximum dose but, of course, this is only delivered to a small portion of the rectum or bladder, and on such grounds a somewhat smaller dose would probably be more appropriate.

Estimation of late-effect data from clinical results

In the light of these uncertainties, we have attempted to estimate the dose (relative to point A) responsible for late effects (*i.e.* the critical normal-tissue dose reduction) directly from clinical data. We note that from Equation (9), if the parameter set $[\alpha_L, \beta_L, \tau_L, \ln(K)]$ is known, and the late-effect probability P is known for a given protocol, the only remaining unknown is the critical normal-tissue dose reduction factor, r. Turesson and Thames (1989) have fitted some clinical results (using external beam therapy where $r = 1$) to Equation (9) and thus estimated the parameters $[\alpha_L, \beta_L, \tau_L, \ln(K)]$ for a clinically observed late skin reaction. Although the late effect (human skin telangiectasia) is different from those of interest here, in the absence of other estimates, we have used these parameter values ($\alpha_L = 0.084\ \text{Gy}^{-1}$, $\beta_L = 0.021\ \text{Gy}^{-2}$, $\ln(K) = 3.6$). For the repair half-time,

Table I. Percentage of point-A dose delivered to normal tissues at risk for late effects during intracavitary brachytherapy of the uterine cervix

Site	Percentage of point-A dose	Reference
Rectum (anterior)	45 ± 12	Bidmead & Stafforth (1985)
	52	Joslin (1989)
	77 ± 29	Krishnan et al (1990)
	56 ± 15	Martel (personal communication (1990))
Rectum (midpoint)	43 ± 15	Krishnan et al (1990)
	35 ± 8	Martel (personal communication (1990))
Rectum (posterior)	27 ± 11	Krishnan et al (1990)
Bladder (posterior)	63 ± 24	Hunter et al (1986)
	103 ± 41	Krishnan et al (1990)
	80 ± 27	Martel (personal communication (1990))
Bladder (midpoint)	57 ± 20	Krishnan et al (1990)
	49 ± 15	Martel (personal communication (1990))
Bladder (anterior)	35 ± 11	Krishnan et al (1990)
Sigmoid	28 ± 7	Bidmead & Stafforth (1985)

Turesson and Thames (1989) report two equally effective repair processes with half-times of 23 and 252 min, and we have adopted these values.

Having the parameter set [α_L, β_L, τ_L, ln(K)], we may estimate the critical normal-tissue dose reduction factor, r, by applying Equation (9) to the late-effect data for cervical brachytherapy reported by Stout and Hunter (1989) and Hunter (personal communication, 1990). These data, from the Christie Hospital, Manchester, are suitable for our purposes because no external beam therapy was used in conjunction with the intracavitary treatment. Their reported complication rate at 4 years for LDR treatment (two weekly fractions, totalling $D_A = 75$ Gy at 0.53 Gy/h) was 8.7 ± 2.5% for grade 2 or 3 reactions. Using Equation (9), a value of r of 0.35 (*i.e.* ~35% of the point-A dose) was found to yield this late-effect probability. This value is in reasonable accord with the proportions summarized in Table I from various estimates in the literature.

As a test of the predictive power of our approach, we have investigated whether we could predict the observed late effects for the higher dose rate arm of the Christie Hospital clinical trial (two fractions, totalling either 60, 65, 70 or 75 Gy, at 1.6 Gy/h). We used the same value of r, the critical normal-tissue dose reduction (0.35) and the same values for the other parameters [α_L, β_L, τ_L, ln(K)]. The results are shown in Fig. 8, and it is clear that we can predict late effects quite well for different doses and dose rates.

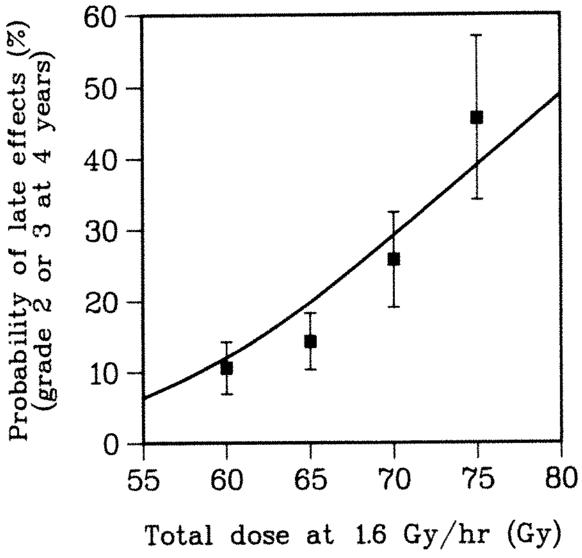

Figure 8. Full curve shows predicted late-effect probabilities for various brachytherapy point-A doses delivered during cervical brachytherapy at 1.6 Gy/h (no external radiation). The dose to the organ(s) responsible for these late effects was taken as 0.35 times the tumour dose to point-A; this value was obtained based on an observed late-effect probability of 8.7% for a point-A dose of 75 Gy and 0.53 Gy/h (Hunter, personal communication (1990)). The points in the figure are results from the Christie Hospital LDR clinical trial for grade 2 or 3 complications after 4 years (Hunter, personal communication (1990)).

Estimation of late effects for HDR intracavitary brachytherapy of the cervix

In light of these successful comparisons where the clinical results at different doses and dose rates are already documented, we make similar estimates of late effects for the HDR regimens that we previously calculated to be equivalent, in terms of early effects (see Figs. 4 and 5), to the LDR scheme of two weekly fractions totalling 75 Gy at 0.53 Gy/h. Using Equation (9), the normal-tissue dose reduction of $r = 0.35$, and the parameters for late effects [α_L, β_L, τ_L, ln(K)], we can predict the late effects from these HDR fractionation schemes. Figure 9 shows the predicted late effects for different fraction numbers, as a function of the HDR dose. The marked star, in each case, corresponds to the dose that was matched (see above) to produce early effects equivalent to those of the LDR regimen. Thus the stars indicate those late effects that would be predicted to occur clinically as a result of the regimens shown in Fig. 5.

It can be seen in Fig. 9 that the use of a critical normal-tissue dose reduction of $r = 0.35$ to calculate late effects implies that, in all the HDR fractionation schemes, predicted late effect probabilities will be less than the 9% that was clinically observed for LDR (and from which our value of $r = 0.35$ was derived). As

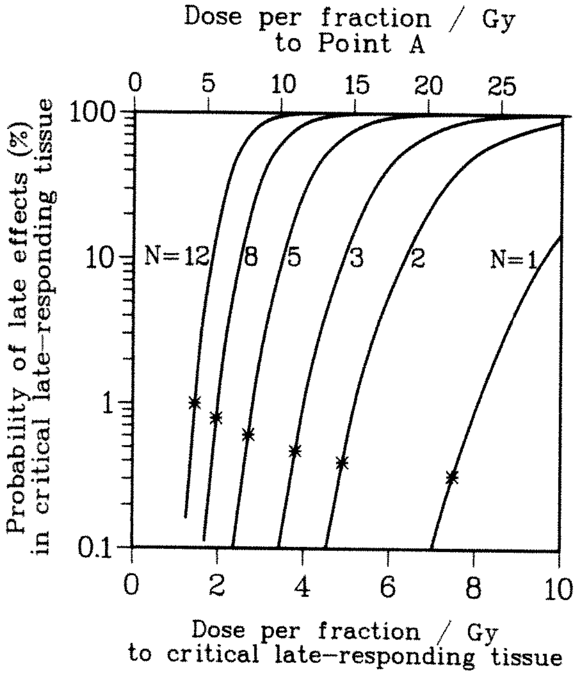

Figure 9. Predicted late effects (grade 2 or 3 complications after 4 years) for different fractionation numbers, as a function of the HDR dose to the critical normal tissue or to the tumour dose to point A. The star, in each case, corresponds to the normal-tissue dose $r \times D_A$, where D_A is the optimized (for early effects) point-A dose for that fraction number, as shown in Fig. 5, and $r = 0.35$. Thus the late effect probabilities indicated by the stars are those that would be predicted to occur for the regimens shown in Fig. 5.

discussed above, any value of r below about 0.5–0.8 (depending on the particular fractionation schemes) will result in late effects for HDR that are not worse than those for LDR, given matched doses for early effects.

In addition to our own estimate of r, the values of the dose reduction given in Table I provide some guidance as to possible r values; an important point to note here is that, by use of suitable applicators, it is quite practical to push critical normal tissues away from the intracavitary radiation sources for the few minutes required for a treatment at HDR, compared with the few days required for an LDR treatment. On the basis of surveys of various centres, Orton (1990) has estimated that an extra $20 \pm 6\%$ dose reduction to the rectum or bladder is typically achieved by retraction techniques during HDR treatment.

Given the ranges of normal-tissue dose reduction factors shown in Table I, as well as an extra dose reduction of about 20% from improved retraction during HDR therapy, it seems likely that values of r yielding worse late effects at HDR relative to LDR will rarely occur in the clinic. In fact, evidence from a recent survey (Orton, personal communication (1990)) of many centres involved in either LDR or HDR brachytherapy of the cervix, indicates that, though 3 and 5 year survival rates are comparable for the two regimens, complication rates are considerably lower for HDR regimes ($13.4 \pm 1.3\%$ for HDR *versus* $22.4 \pm 3.0\%$ for LDR, for moderate and severe complications). These data lend support to the notions discussed here.

Figure 9 also demonstrates, for doses matched to produce equal early effects, late-effect risks decreasing as the fraction number decreases, even down to a single fraction. Whilst this follows from the formalism outlined here, it should be noted that late-effect reduction is not the only criterion of importance when deciding on the optimal number of fractions. For example, the use of too few fractions may impair tumour control because of inadequate reoxygenation. For this reason alone, although the use of smaller numbers of HDR fractions has been suggested (see Fig. 6), it appears inexpedient to consider treating with less than about five fractions.

A final point from Fig. 9 is to note that these calculations are for brachytherapy alone, *i.e.* without an external boost. Clearly, when an external whole pelvic dose of ~45 Gy is added to a brachytherapy regime, the ratio of the critical normal tissue dose to the prescribed total dose will worsen (*i.e.* increase). From results at Columbia-Presbyterian Hospital (Martel, personal communication (1990)) the mean dose to the mid-rectum relative to point A was 0.35 ± 0.08 for LDR brachytherapy alone, but increased to 0.71 ± 0.06 for the total treatment of brachytherapy plus external whole-pelvic irradiation. For HDR treatment this increase can, as discussed above, be partially mitigated by improved retraction.

Conclusions

We have shown that it is possible to use experimental data obtained *in vitro* and *in vivo* to estimate doses that, given in a few large fractions at HDR, may be equivalent to LDR insertions in the intracavitary treatment of carcinoma of the uterine cervix. Other factors, such as the need to provide adequate time for reoxygenation of hypoxic tumour cells, may make it imprudent to consider less than about five fractions.

Whilst, in general, use of a few large fractions results in a greater risk of late effects than LDR, intracavitary brachytherapy of the cervix may be an exception, because the dose to critical late-responding normal tissues is less than the prescribed dose upon which tumour control depends.

There are two separate factors involved here, one physical and one radiobiological. First, by the use of appropriate applicators and packing it is more practical to retract critical normal tissues further from the radioactive sources, and so reduce the dose to these tissues for the brief duration of an HDR treatment, compared with the long irradiation times at LDR (Orton, 1990). This constitutes a physical factor. Second, if the doses to be used in HDR and LDR treatments are matched for early effects at the full prescribed dose, then the HDR regime does not necessarily produce worse late effects at a dose which is less than the prescribed dose, since the dose–response relation at HDR has a more pronounced curvature than at LDR. This is a radiobiological factor which, in fact, will be enhanced by the physical factor, *i.e.* the decreased HDR dose to critical organs relative to the prescribed dose.

It seems likely, therefore, that an HDR intracavitary protocol consisting of about five fractions, the doses in which are based on matching early effects to LDR, will result in similar survival and no worse late effects compared with LDR. Preliminary clinical results of HDR trials appear to support this notion. Calculations for equivalent HDR regimes to many LDR regimes in current use, including the effect of external teletherapy, are presented elsewhere (Brenner & Hall, 1990).

Acknowledgments

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Acute response of mouse kidney clonogens to fractionated irradiation *in situ* and then assayed in primary culture

By Yee-Min Jen, MB and Jolyon H. Hendry, PhD

Cancer Research Campaign Department of Radiobiology, Paterson Institute for Cancer Research, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, UK

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Abstract. Although the difference in sensitivity to the changes in dose fraction size between early-responding and late-responding tissues is well established, the underlying mechanisms in terms of target-cell responses are not yet clearly identified for any tissue. The radiosensitivity of mouse kidney cells after *in situ* single-dose, 2, 8, and 16 fraction X-irradiations was measured in primary culture using a clonogenic assay. The assay was made 12 h after single doses or 12 h after the last dose of the multifraction regimens. When analysed using the linear–quadratic model, as predicted the individual α components for all the different fractionation schedules were not significantly different, and the changes in the β values were consistent with those expected on the basis of the reciprocal fraction numbers. When all four data sets were integrated to derive a common α/β ratio, the result was 4.4 ± 1.3 (1SE) Gy, or 2.8 ± 0.9 Gy (a better fit) if the single-dose data set was excluded. These values fall into the range reported for kidney using assays of tissue function at long times after irradiation. Hence, it has been shown for the first time that the fractionation sensitivity of a late-responding organ is mimicked by that of a clonogenic cell population in that organ. The evidence also suggests that the time available prior to fixation of potentially lethal damage does not influence the low α/β ratio observed for the kidney.

A systematic difference for early and late effects in normal tissues has been shown in the isoeffect curves relating the total dose and the dose fraction needed to reach a given level of tissue response (Thames et al, 1982). Since then it has been accepted that for early responses in tissues, the α/β ratio is between 5 and 20 Gy, and for late reactions it is usually 2–5 Gy (Fowler, 1984; Thames & Hendry, 1987). This dissociation of fractionation sensitivities has been attributed variously to differences between the respective target-cell populations in (a) inherent radiosensitivity (Thames et al, 1982), (b) cell cycle distribution (Zeman & Bedford, 1984; Schultheiss et al, 1987), (c) different tissue organizations (Wheldon et al, 1982; Wheldon & Michalowski, 1986), and (d) repair rate and time available before fixation of potentially lethal damage (Thames, 1985; Curtis, 1987; Curtis & Thames, 1989). However, owing to the difficulties in identifying the relevant target cells and their cycling characteristics (Hendry & Potten, 1988), there has been a lack of corresponding information at a cellular level to test the interrelationship between the response of the tissue and the putative target cells.

The idea of the possible importance of differences in the time available before fixation of potentially lethal damage was tested using the liver, assaying clonogens using a transplantation technique 1 day or 10 months after fractionated irradiation *in situ* (Fisher & Hendry, 1988). The α/β value for this system was in the range 1–2 Gy, and although β tended to decrease with increasing time there was little overall change in the α/β ratio with increasing intervals available for repair. Little change in the α/β ratio was also reported for kidney using functional assessments of tissue injury at different times after irradiation (Stewart et al, 1984; van Rongen et al, 1988). In addition, Hill et al (1989) found that the α/β ratio for mouse stroma in the tumour bed effect remained unchanged when the expression of stromal injury was stimulated within 3 days or 6 months.

Using various renal function assays, studies of response after single-dose and multifraction irradiations have been conducted and α/β ratios of 2.6–3.7 Gy (Stewart et al, 1984), 0–3.5 Gy (Williams & Denekamp, 1984), 0.6–3.8 Gy (van Rongen et al, 1988b), and 2–5 Gy using low fraction sizes (Joiner & Johns, 1988) have been reported in rodents. However, by applying uranyl nitrate to irradiated mouse kidneys in order to precipitate an acute tubular toxicity and regeneration, an α/β value of 12.5 Gy was obtained using a tubule-regeneration assay *in situ* (Ewen & Hendry, 1989a). This suggested that for this kidney system, the time of assay might contribute to the value of the α/β ratio.

In order to investigate this further, a primary-culture colony assay has now been applied to the study of dose fractionation effects *in situ* for one cell population in the mouse kidney, although it is recognized that the importance of this cell population in kidney injury has not yet been established. The acute response of kidney clonogens was assayed 12 h after completion of fractionated irradiation to see if the linear–quadratic model applied well to the data, and if the α/β ratio was similar to the values reported for late responses measured using assays

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Address correspondence to Dr Yee-Min Jen.

of tissue functions, or whether it fell within the higher range reported for acute-responding tissues. Although the proportion of total kidney cells in the S phase is low (Wilson et al, 1987; Ewen & Hendry, 1990), the possibilities that the S phase cells contribute to a significant fraction of the clonogen population, and that this proportion might change during the multifraction irradiations thus involving cell progression effects on radiosensitivity, were studied directly using the tritiated-thymidine cell-suicide technique.

Materials and methods

Animals and irradiations

The mice used were male BDF_1, 11–13 weeks old. The mice were confined in a Perspex jig which rested on a lead shield 3 mm thick with a single port 28×18 mm^2 in size carefully positioned to cover both kidneys, and the mice were confined in a Perspex jig which rested on a anterior–posterior axis. A 300 kVp Pantak X-ray unit fitted with a beam-hardening filter giving a half value layer of 2.3 mm Cu, and with a dose rate of 110 cGy/min was used.

For the split-dose experiment, two equal doses of 6 Gy were given separated with intervals of 0, 2, 4, 6, 8, 12, 18 and 24 h. The kidneys were removed and assayed immediately after the second doses.

For single-dose experiments, a series of graded doses was given, and the mice were killed 12 h after irradiation. For multifraction irradiations, 2, 8, and 16 fractions were given with an interval of 12 h between each dose to allow full recovery, and the irradiations were completed within 1, 4, or 8 consecutive days. The mice were then killed 12 h after the last dose.

Single cell suspensions and culture

The disaggregation procedure, the culture system and the confirmation of the epithelial nature of the colonies have been described in detail previously (Jen et al, 1990). Briefly, the kidneys were removed immediately after the mice were killed. The kidneys were then disaggregated into single-cell suspensions. The kidneys were decapsulated, dissected into pieces, and fragmented using a tissue homogenizer. The tissue was then incubated in the first enzyme cocktail comprising 150 μg/ml collagenase II (Sigma), 0.05 mg/ml deoxyribonuclease I (Sigma), and 0.05 mg/ml pronase (Boehringer Mannheim) for 35 min, followed by a second dispersion cocktail consisting of 0.05% trypsin (Worthington), 0.01% deoxyribonuclease I (Sigma), 0.2% EDTA (BDH Chemical Ltd), and 0.1% bovine serum albumin (Sigma) in Hank's balanced salt solution (Gibco) for 5 min. The cell suspension was pipetted and filtered to produce a single cell suspension. The cell number was determined by counting all nucleated cells which excluded trypan blue. The cells were then cultured at 37°C in 5% CO_2 in air in 25 cm^2 flasks containing 6×10^4 lethally irradiated 3T3 feeder cells in F12 + Dulbecco's modified Eagle medium, Gibco (SFFD) + 10% fetal calf serum. Colonies with more than 50 cells were counted after 10 days' growth.

Cell suicide experiments

The proportion of S phase kidney clonogens was measured in unirradiated mice and in mice after receiving 30 Gy in a 16 fraction schedule with 2 fractions per day and an interval of 12 h. Tritiated thymidine ([^{3}H]TdR, specific activity: 740 GBq/mmol, Du Pont) was used in a method developed for haemopoietic clonogens (*e.g.* Lord & Schofield, 1985). Cell suspensions of around 4×10^6 cells/ml were divided into control and experimental tubes. Tritiated thymidine was added to the experimental tube to make the final activity of the suspension 3.7 MBq/ml. An equal volume of medium was added to the control tube. The cells were then incubated at 37°C for 30 min. At the end of the incubation, ice-cold thymidine was added, followed by centrifugation. This washing procedure was repeated three times to remove residual radioactivity. The cells were then assayed for survival as described above. The number of colonies in the control and experimental tubes were then compared. Total colony counts per culture were maintained above 2000 to detect with 90% probability a percentage as low as 10% S phase clonogens (Hazout & Valleron, 1977).

Analysis of survival data

Each data set from 1, 2, 8, and 16 fraction regimens was fitted to obtain its individual survival parameters using a computer program and the linear–quadratic (LQ) model (Roberts, 1990). The program calculated a best-fit curve using maximum likelihood techniques and gave values for α, β, and α/β. After n fractions of dose d to a total dose of D, $-\ln \mathrm{SF} = \alpha D + (\beta/n)D^2$. Hence, according to the LQ model, the α component should remain constant regardless of the fraction number, while the β component changes by a factor of $1/n$. The α/β ratio would then change by a factor of n. The values of $[(\alpha/\beta) \times (1/n)]$ were thus calculated for each fractionation schedule.

If the presumption holds that every dose in a multifraction irradiation is equally effective, the equivalent survival of one fraction out of a total fractionated dose should be the overall survival from that regimen to the power of the reciprocal of the fraction number (*e.g.* $\mathrm{SF}^{1/16}$). In practice, in order to allow appropriate weighting of the data points, equivalent single-dose survivals for 2, 8, and 16 fraction irradiations were calculated by leaving the colony numbers as measured and reducing the number of cells plated N by the power of the reciprocal of the fraction number (*e.g.* $N^{1/16}$). All data were then fitted to the LQ model to obtain an overall value of α/β.

Analysis of variance using an F test was performed to determine the statistical significance of the difference between two sets of survival parameters.

Results

The fraction of epithelial-type colonies was 85–95% with and without 12 Gy single-dose irradiation (Jen et al, 1990), and it was similar when measured after 16 Gy in eight fractions.

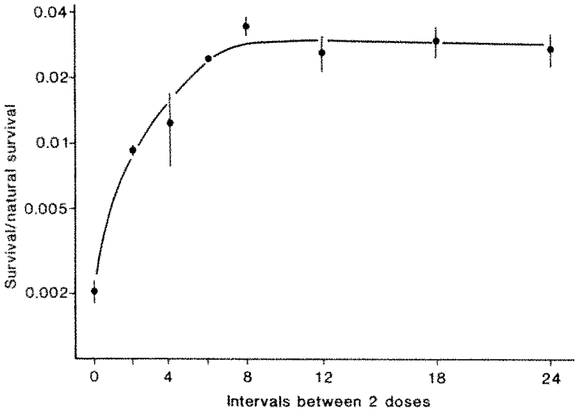

Figure 1. Survival divided by natural survival (*i.e.* surviving fraction) in a split-dose experiment using two equal doses of 6 Gy separated by intervals of 0, 2, 4, 6, 8, 12, 18 and 24 hours. The plateau was reached after an interval of 6–8 hours, and was unchanged up to 24 hours. Errors representing 1 SE are shown when larger than the symbols.

The split-dose experiment shows that recovery had reached a plateau after an interval of 6–8 h (Fig. 1). No further increases in survival was detected with increasing intervals up to 24 h.

All four data sets were fitted separately (Fig. 2) or with a common α value of $0.11 \pm 0.02\ \mathrm{Gy}^{-1}$, and in both cases the data well fitted the LQ model. The two fittings were not significantly different ($p = 0.8$). The individual values for α, β, and $(\alpha/\beta)(1/n)$ are presented in Table I. The α/β ratio for single-dose irradiation was 4.7 ± 3.5 Gy, with a value for α of $0.11 \pm 0.06\ \mathrm{Gy}^{-1}$. There was a tendency for both the mean and the standard error of the α/β ratios to increase as the fraction number increased. The $(\alpha/\beta)(1/n)$ values were not significantly different from each other and fell in the range 4–5 Gy.

When the converted single-dose equivalents were analysed together with the single-dose data set to derive a common α-β value, the value was 4.4 ± 1.3 Gy, while it was 2.8 ± 0.9 Gy when the single-dose data set was excluded (Fig. 3). The fitting excluding the single dose data set was a significantly better fit ($p < 0.0001$).

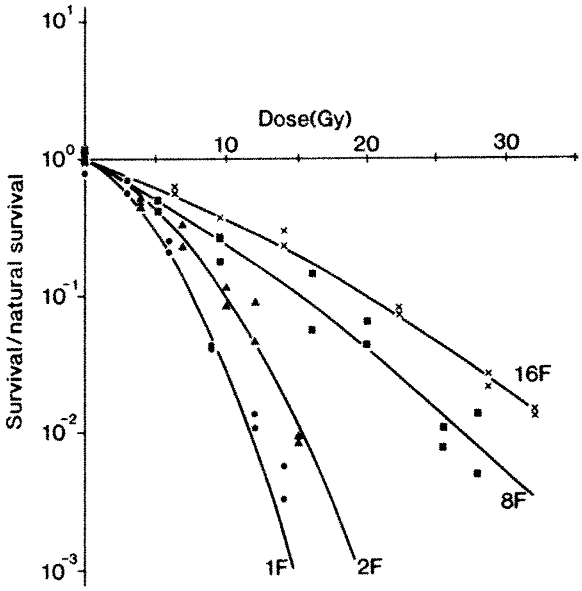

Figure 2. Fractionated-dose survival curves for kidney clonogens. When the individual data sets were fitted separately using the LQ model, the α components were not different from each other (for values see Table I). The β component changed approximately by a factor of reciprocal fraction number. The values of $(\alpha/\beta)(1/n)$, which represent the true α/β ratio irrespective of fraction number, were about 4–5 Gy: ●, single dose; ▲, 2 fractions; ■, 8 fractions; **x**, 16 fractions. Each curve was constructed from two independent experiments for most of the doses.

The suicide data showed that not more than a few per cent of clonogens were in S phase, either in control mice or at the end of the fractionation schedule (Table II).

Discussion

The present work has shown that the initial phase of recovery is completed after an interval of about 6–8 h (Fig. 1). Guichard et al (1982), in a similar experiment, reported an increased surviving fraction from 0 to 1.5 h interval and subsequently the level remained unchanged up to a 24 h interval. Repair half-times assessed using assays of tissue functions have been reported to be in the

Table I. Survival parameters using the LQ model for kidney clonogens 12 h after single and fractionated irradiations

	1F	2F	8F	16F
α (Gy^{-1})	0.11 ± 0.06	0.10 ± 0.05	0.13 ± 0.03	0.089 ± 0.025
β (Gy^{-2})	0.024 ± 0.006 (0.025 ± 0.002)	0.013 ± 0.004 (0.013 ± 0.002)	0.0015 ± 0.0010 (0.0027 ± 0.0007)	0.0014 ± 0.0007 (0.0011 ± 0.005)
$(\alpha/\beta)(1/n)$ (Gy)	4.7 ± 3.5 (4.2 ± 0.96)	3.7 ± 3.0 (4.2 ± 1.1)	10.5 ± 9.7 (5.4 ± 2.3)	4.0 ± 3.2 (7.3 ± 5.1)

Figures in parenthesis represent parameters obtained using a common α of $0.11 \pm 0.02\ \mathrm{Gy}^{-1}$ for the LQ model fitting. The common α/β ratio describing all the fractionation and single-dose data sets is 4.4 ± 1.3 Gy, and 2.8 ± 0.9 Gy when the single-dose data set is excluded. All errors are 1 SE.

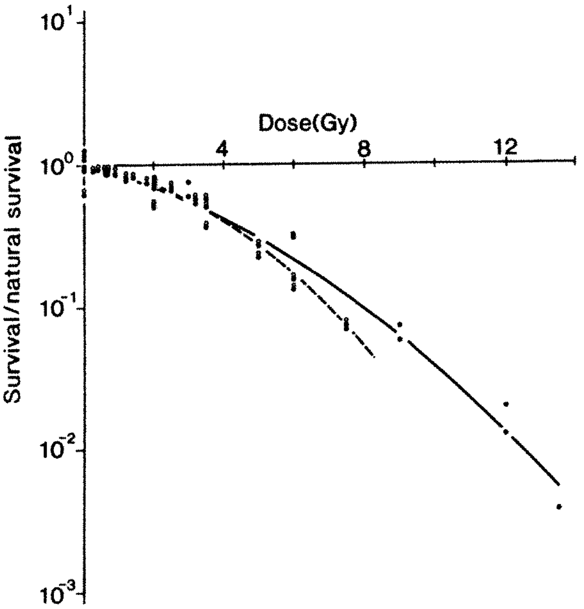

Figure 3. Survival curve for kidney clonogens. With the presumption that each dose in a multifraction irradiation is equally effective, the equivalent survival of one fraction out of a total fractionated dose should be the overall survival to the power of the reciprocal of the fraction number. Using this conversion, equivalent single-dose survivals for 2, 8, and 16 fraction regimens were calculated (see text) and fitted to the LQ model to obtain an overall α/β ratio characterizing all the data sets. The value was 4.4 ± 1.3 Gy when the single-dose data set was included (———), and 2.8 ± 0.9 Gy when excluded (– – –). The fitting excluding the single-dose data set was a significantly better fit ($p < 0.0001$).

range 1.5–2.1 h, depending on the fraction number and type of function assessed (van Rongen et al, 1990). Also, using assays of tissue functions, the recovery half-times were 0.92 ± 0.10 (95% CL) h for 7 + 7 Gy split doses and 1.69 ± 0.39 h for 18 × 2 Gy (Rojas & Joiner, 1989). As four half-times would give a near completion of repair, the present observation of 6–8 h is similar to those using functional assays. The reason for the shorter repair time reported by Guichard et al (1982) is not clear.

In order to provide enough time for repair between fractions and still keep a constant interval between any two doses in a multifraction schedule, an interval of 12 h was chosen. In the single-dose experiment, a delay of 12 h before assay was also allowed. The α/β ratio of 4.7 ± 3.5 Gy assayed 12 h after single-dose irradiation in the present study is significantly different from the value of 0 ± 1.57 Gy found using the same system but assayed immediately after irradiation (Jen et al, 1990). Also, the β value of $0.025 \pm 0.002\ \mathrm{Gy}^{-2}$ for the 12-h delay assay is smaller than the value of $0.045 \pm 0.007\ \mathrm{Gy}^{-2}$ for the immediate assay. Such *in situ* repair phenomena have been reported in the mammary gland (Gould & Clifton, 1979; Mahler et al, 1983), the thyroid (Mulcahy et al, 1980), the liver (Jirtle et al, 1982; Fisher et al, 1988), and the kidney (Jen et al, 1990). With longer assay times, it has been observed in liver that β decreases, and the α/β value increases, though not markedly, with a 14-week to 10-month delay of assay (Fisher & Hendry, 1988). This effect can also be seen in some of the other studies using assays of tissue function (Table III). These data do not support the hypothesis that the repair time available before assay may account for the generally low α/β ratio in late-responding tissues (Thames, 1985; Curtis, 1987; Curtis & Thames, 1989). Nevertheless, the observations do suggest that repair of potentially lethal damage, and thus post-irradiation conditions, may well play a role not only in the absolute values of α and β but also consequently in the values of the α/β ratio.

According to the LQ model, the α component should remain the same regardless of the fraction number, and the α/β ratio for different fractionated regimens of n fractions should change by a factor of n. The present results were in agreement with these predictions (see Table I). When a constant α was adopted, the values of $(\alpha/\beta)(1/n)$ were 4.2 ± 0.96, 4.2 ± 1.1, 5.4 ± 2.3, and 7.3 ± 5.1 Gy for the 1, 2, 8 and 16 fraction irradiation schedules. None of the values was significantly different from each other.

The equivalent-single-dose conversion for calculating an α/β ratio has been used for analysis of functional assays (Stewart et al, 1984). In order to obtain an α/β ratio using all the data from various fractionation schedules, this method was also applied in the present study. Here, the LQ model again fitted fairly well to the fractionation survival data. However, when the single-

Table II. Mean colony number ± SE per flask in two cell-suicide experiments for unirradiated kidneys and kidneys after receiving 30 Gy in 8 days; for each group 15 flasks were used, and a total of over 2000 colonies were counted

	Experiment 1			Experiment 2		
	$-{}^3$HTdR	$+{}^3$HTdR	% kill	$-{}^3$HTdR	$+{}^3$HTdR	% kill
No irradiation	198.7 ± 2.6	201.9 ± 3.1	≤ 0	283.3 ± 5.1	276.8 ± 4.8	2.3 ± 2.2
30 Gy	204 ± 4.5	212.8 ± 6.0	≤ 0	197.8 ± 3.0	197.3 ± 3.4	≤ 0

$p > 0.1$ for all comparisons between control and experimental data.

Table III. α/β ratios for mouse tissues obtained using different times of assay

Tissues	Assay	Time of assay	α/β (Gy)	References
Kidney	Urine output	19 weeks	3.27 ± 0.26	Stewart et al, 1984
		22 weeks	3.61 ± 0134	
		26 weeks	2.80 ± 0.22	
		32 weeks	2.63 ± 0.26	
		36 weeks	2.75 ± 0.37	
	EDTA clearance	19 weeks	3.39 ± 0.20	
		22 weeks	3.73 ± 0.20	
		26 weeks	3.21 ± 0.12	
		36 weeks	2.68 ± 0.17	
Kidney	Histological	6 months	0.17, 0.58	Jordan et al, 1985
		12 months	1.4	
Kidney (data for 10–40 fractions)	Serum urea	12 weeks	3.75 (1.35, 5.03)	van Rongen et al, 1988
		32–36 weeks	3.62 (2.07, 5.98)	
	Urine osmolality	12 weeks	0.92 (–0.17, 2.78)	
		32–36 weeks	2.77 (1.60, 5.12)	
	Urine volume	12 weeks	2.32 (0.57, 6.64)	
		32–36 weeks	2.94 (1.74, 5.51)	
Liver	Transplantation of hepatocytes to fat pads	1 day	1.0–1.6	Fisher & Hendry, 1988
		14 weeks	1.3–1.6	
		10 months	1.9–2.1	
Dorsal subcutaneous stroma	Tumour bed effect, 15 Gy single-dose equivalent	1–3 days	4.98 ± 0.82	Hill et al, 1989
		6 months	4.74 ± 1.43	
	17 Gy single-dose equivalent	1–3 days	4.58 ± 0.93	
		6 months	5.96 ± 1.81	

Figures in parenthesis indicate 95% confidence limits.

dose data set was excluded in the analysis, the α/β ratio was 2.8 ± 0.9 Gy, and this was a significantly better fit $(p < 0.0001)$ than the value of 4.4 ± 1.3 Gy when the single-dose data set was included. Using rats, with the left kidney irradiated and a right nephrectomy, van Rongen et al (1988b) noted a poor fit of their tissue-function data to the LQ model. They noticed an improved fit when the single-dose data were omitted. The incompatibility between the single-dose data set and the fractionation data has also been reported in liver using a transplantation assay (Fisher & Hendry, 1988). In the present study, single doses larger than 9 Gy and survival values smaller than 10^{-2} produce the deviations (Fig. 3). This is in agreement with considerations of survival models where the α, β formulation is an approximation to models with more parameters, *e.g.* Gilbert et al (1980), Barendsen (1982), Thames (1985), and Curtis (1987).

The response of kidney to radiation has been studied extensively using functional and histological assays. For functional assays to be able to detect the radiation response of adult animals with bilateral kidney irradiation, assay times of 8–12 or 14–19 weeks for the mouse (Glatstein, 1973; Williams & Denekamp, 1984), 4 or 12 weeks for the rat (Smith & Boss, 1957; Jongejan et al, 1987), were needed. For histological assays, it was 3–5 weeks for mild vascular and tubular changes in the dog (Hoopes et al, 1986), 4 or 12 weeks for early signs in the mouse (Michalowski et al, 1986; Glatstein et al, 1977), and 60–68 weeks or over 50 weeks for late changes in the mouse (Withers et al, 1986; Ewen & Hendry, 1989b). No significant change in the α/β ratio was observed with different delays before assay (van Rongen et al, 1988) (Table III), although by using a histological grading method, Jordan et al (1985) reported a good fitting of their data to the LQ model giving an α/β ratio of 0.17 and 0.58 Gy when assayed at 6 months, but a poor fit with an α/β ratio of 1.4 Gy when assayed at 12 months. When comparing the low α/β values from the present fractionation study and those using functional assays, and considering the *in situ* repair phenomenon discussed above, the evidence suggests that the difference in α/β ratios between acute-responding and late-responding tissues may reside more probably in the status or changing status of the target cells during the irradiation schedule, *i.e.* any difference in cell cycle distribution, tissue organization, or intrinsic differences in radiosensitivity. The reason for the high α/β ratio of 12.5 Gy for mouse kidney assayed acutely using a tubule-regeneration technique (Ewen & Hendry, 1989a) remains elusive. It may relate to the use of the cytotoxic chemical uranyl nitrate to stimulate proliferation and possibly affecting repair, or to the number of cell divisions induced. There is also other evidence showing that α/β ratios for the colony-forming cells of early-responding tissues are lower when irradiated using split doses in their slowly cycling state, and higher when given fractionated irradiations where cycling may be increased (Hendry & Potten, 1988). However, using the thymidine suicide technique in the present study, S phase clonogens were not found in significant proportions either before or after irradiation. Hence, there was no marked change in the very low cycling status which might influence the sensitivity to later dose fractions and hence change the α/β ratio.

Although a dose-per-fraction dependent effect on the division potential of lethally irradiated cells might lead to a dissociation between functional and clonogenic endpoints, as a few divisions might be important in functional but not in clonogenic assays (Wheldon et al, 1982; Thames et al, 1986), the α/β ratio of about 3 Gy from the present study resembles that using functional assays of 0–4 Gy (Stewart et al, 1984; Williams & Denekamp, 1984; Joiner & Johns, 1988; van Rongen et al, 1988). While for several hierarchical tissues, tissue effects have been correlated to target cell responses (*e.g.* Hendry et al, 1983; Thames & Hendry, 1987), such a correlation has not been established for kidney and other late-responding tissues although some of the possibilities have been explored (Travis & Tucker, 1986; Withers et al, 1986; Thames et al, 1989; Tucker & Hendry, 1990). Although the target cells for the functional responses of the kidney are not precisely known (Williams, 1986; Robbins & Hopewell, 1987), the present data are the first which show that the fractionation sensitivity of a late-responding organ is mimicked by that of a clonogenic cell population in that organ.

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The composition of body tissues

(II) Fetus to young adult

By D. R. White, PhD, *E. M. Widdowson, FRS, DSc, †H. Q. Woodard, PhD and §J. W. T. Dickerson, PhD

Radiation Physics Department, St Bartholomew's Hospital, London EC1A 7BE, *Department of Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK, †Department of Biophysics, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, NY10021, USA and §Department of Biochemistry, University of Surrey, Guildford GU2 5XH, UK

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Abstract. The composition of body tissues is a function of the age, nutrition, state of health and physical activity of the individual. In this paper, the effects of *age* on the composition of *healthy* tissues are reviewed. Eleven soft tissues (adipose tissue, blood—whole, brain—whole, heart, kidney, liver, lung, muscle—skeletal, placenta, skin and spleen) and cortical bone are considered. Elemental compositions, mass and electron densities are tabulated for the tissues, as a function of age, from fetus to young adult. Although the compositions given here are predominantly for healthy tissues, reported changes because of dietary influences are briefly discussed.

The chemical development of the body is a continuous process before and after birth, and in most respects there is no sudden change at the time of birth (Widdowson & Dickerson, 1964). For this reason changes in the composition of the body should be considered from early in fetal development until the age when growth has ceased. This paper is one in a series reassessing the available data on the composition of body tissues of healthy individuals (Woodard & White, 1986). The present paper is concerned with body tissues from fetal life to young adulthood.

The data on organ composition reviewed were derived from computer-assisted library searches. Unpublished measurements made by three of the authors (E.M.W., H.Q.W. and J.W.T.D.) and by Southgate (1988, Personal communication) were included in the analyses.

Results are presented here for adipose tissue, whole blood, whole brain, heart, kidney, liver, lung, skeletal muscle, placenta, skin and spleen at selected ages between 14 weeks gestation and 18 years. In addition, data for cortical bone are given at representative ages between 20 weeks gestation and 18 years. For purposes of comparison, the compositions of cortical bone for adults from 20 to 90 years are presented graphically. Water, lipid, protein, carbohydrate and mineral contents, elemental composition, mass and electron densities are tabulated for each of the body tissues identified. All the values presented are for *healthy* human tissues.

The following terminology has been adopted. A *fetus* is aged between 8 and 40 weeks from conception. In this paper, composition data are included for fetal tissues covering the age interval 14 weeks gestation to term. All references to a *newborn* infant are for a 40-week, full-term fetus. An infant is less than one year of age (DHSS, 1980). The infant then becomes a *child*. A *young adult* is assumed to be approximately 18 years of age.

It is hoped that these results will be of value in both theoretical and experimental radiation dosimetry. The compositions facilitate the production of tissue substitutes essential to the manufacture of infant and child phantoms for use in radiodiagnosis and radiotherapy. The study further illustrates how the composition of the adult body and its tissues is ultimately achieved.

Materials and methods

The body tissues considered in this study fall naturally into two categories, *soft tissues* and *skeletal tissues*. The sources of composition data used are shown in Table I. Unless stated to the contrary, compositions for soft tissues cover the age interval from a 14-week fetus to a young adult.

A graphical method was used to establish the relationship between the components (water, lipid, protein, etc.) of each tissue and the age of the individual. This is illustrated in Figs 1, 2, 3 and 4, which show the available data for adipose tissue, muscle—skeletal and cortical bone, respectively. Whenever possible, the relationship was established by regression analyses (*e.g.* muscle—skeletal, cortical bone). When these analyses appeared inappropriate (*e.g.* adipose tissue), mean values of the components were derived within defined age intervals. The subsequent analytical procedure was similar to that given by Woodard & White (1986). For convenience, the principal steps in the procedure are given below.

(a) Water, lipid, protein and carbohydrate contents ($\geqslant 0.1\%$, by mass) were compiled.
(b) The concentrations ($\geqslant 0.1\%$, by mass) of elements with $Z > 8$ were similarly compiled.

Table I. Sources of composition data

Body tissue	Reference	Comments
Soft tissues		
Adipose tissue	Dju, 1953, 1988; Thomas, 1962; Baker, 1969	Composition data from birth to 18 years of age available. No results for fetal adipose tissue, although combined skin and subcutaneous adipose tissue layer covering fetus has been analysed (Widdowson, 1988)
Blood—whole	Wintrobe & Shumacker, 1936; McCance & Widdowson, 1956; Widdowson & McCance, 1956; Documenta Geigy, 1970, 1984	The composition of whole blood for the fetus, newborn baby and adult are considered
Brain—whole	Dju, 1953, 1988; Himwich & Himwich, 1957; Widdowson & Dickerson, 1960; Garrow et al, 1965; Fillerup & Mead, 1967; Rosso et al, 1970; Dickerson, 1988; Southgate, 1988	Information available on whole brain and not on separate grey and white matter
Heart	Dju, 1953, 1988; Widdowson & Dickerson, 1960; Widdowson, 1988; Southgate, 1988	Heart muscle is considered
Kidney	As for heart	
Liver	Imrie, 1914; Dju, 1953, 1988; Emery & Finch, 1954; Widdowson & Dickerson, 1960; Garrow et al, 1965; Southgate, 1988; Widdowson, 1988	
Lung	Southgate, 1988; Widdowson, 1988	Only data for the fetal lung (17–40 weeks)
Muscle—skeletal	Dju, 1953, 1988; Dickerson & Widdowson, 1960; Cheek, 1968; Elliott & Cheek, 1968	The results appropriate to skeletal (striated) muscle included
Placenta	Southgate, 1988; Widdowson, 1988	The 14–40-week placenta is considered
Skin	Dju, 1953, 1988; Widdowson & Dickerson, 1960	Only data for 14-week-old fetus to full-term newborn considered
Spleen	Southgate, 1988; Widdowson, 1988	Only data for 26-week-old fetus to full-term newborn considered
Skeletal tissues		
Cortical bone	Dickerson, 1962, 1988; Woodard, 1962, 1964, 1988	Composition available from 20-week-old fetus to 90-year-old adult. Water content not quoted in original paper by Dickerson (1962)

(c) A single mean composition was established. In the case of adipose tissue, three sets of compositions were calculated once the mean (M) and standard deviation (σ) of each component were established, corresponding, to $M-\sigma$, M and $M+\sigma$.

(d) The derived composition was corrected by 100% mass by allocating any missing mass to the major ($\geq 75\%$) component or proportionally between several major components when each were $< 75\%$. Corrections for excess mass were carried out in a similar fashion. For most soft tissues the major component was water; for adipose tissue it was lipid. In cortical bone the mass unaccounted for was assumed to be carbohydrate which was known to be present in small amounts, but was not measured directly.

(e) The elemental composition was then calculated from the elemental compositions of the components given by Woodard & White (1986).

(f) The mass density was estimated from the mass proportions and the mass densities of the components (Brožek et al, 1963; Fomon, 1966). The mass density of a material such as protein when it is in combination with other constituents *in vivo*, may differ from its density in crystalline form *in vitro*. Hence, the mass densities calculated here may differ from the actual densities in the living body. Unfortunately, measured values were not available for most of the tissues considered, so it was necessary to use estimated values. The errors involved are not likely to exceed a few per cent.

(g) Mass and volume electron densities were then calculated using Avogadro's Constant (6.022045×10^{26} kmol^{-1}) (CRC, 1987) and the accepted mass density of the body tissue.

Results

Tables II and III show the results for the soft tissues, arranged in alphabetical order. The water, lipid, protein, carbohydrate and mineral contents (%, by mass) are given in Table II, while the elemental compositions (%, by mass) are listed in Table III. The results for cortical

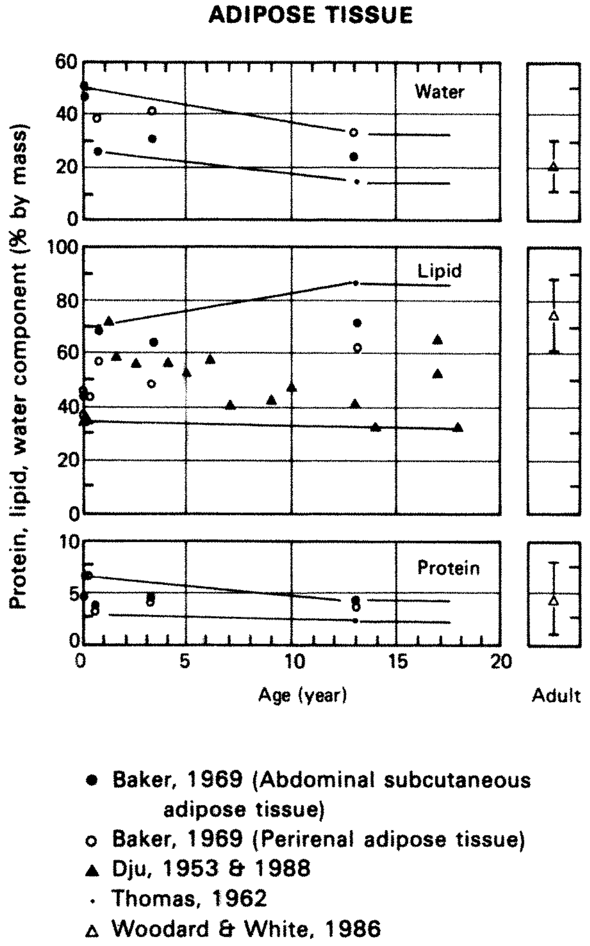

Figure 1. Plots of protein, lipid and water content *versus* age for adipose tissue. Graphs indicate extremes of plotted values. Data for the adult are from Woodard and White (1986).

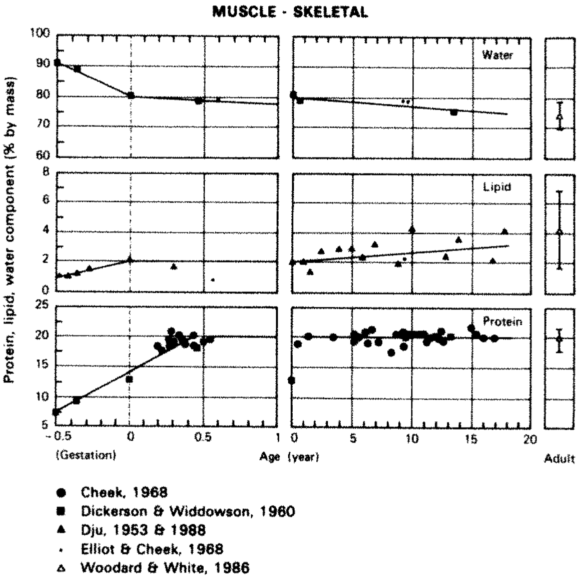

Figure 2. Plots of protein, lipid and water content versus age for muscle—skeletal. Some of the points on the −0.5 to +1 year graphs are also plotted on the 0 to 18 year graphs. Graphs are fitted to plotted values. Data for the adult are from Woodard and White (1986).

bone are given in Tables IV and V. For completeness, the elemental compositions of adult tissues which are given by Woodard & White (1986) are listed in the tables.

Soft tissues

Adipose tissue. Adipose tissue is the most variable component of the body, especially as regards the contribution it makes to the body mass. Most of the lipid in the body is triglyceride in the adipose tissue under the skin and around the internal organs.

In the human body, lipid is deposited quite rapidly during the last trimester of pregnancy so that the body of the full-term infant contains about 14% lipid, by mass. Apart from triglycerides, complex lipids are important components of cell membranes and these lipids are thus an integral part of each organ. In the brain complex lipids increase with the process of myelination (*vide infra*). Fatty infiltration may occur in many organs and tissues as a result of malnutrition or other dietary disturbances.

The composition of adipose tissue also varies considerably. Like other tissues, the percentage of water decreases as the lipid and protein increase. In children and adults the composition of adipose tissue varies with the total amount of lipid in the body. Adipose tissue of fatter individuals has a higher lipid concentration and less water than that of leaner individuals (see Discussion).

Blood—whole. The proteins of whole blood are haemoglobin and the serum proteins, albumens and globulins. Both haemoglobin and serum proteins change in concentration with age. The concentration of haemoglobin in fetal blood is low, rises to a maximum at term, and falls rapidly thereafter so that by 6 months it is little more than half its value at birth. It then rises slowly throughout childhood to reach its adult value at puberty. The concentration of haemoglobin in the blood of men is about 2 g/100 ml higher than in the blood of women. Although iron is recognized as the element essential to the oxygen-carrying capacity of the blood and has a high atomic number ($Z = 26$), it contributes only about 0.1% to the total blood mass and so is not of great radiological importance.

The concentration of protein in serum is also low in the fetus and rises during fetal life; it continues to rise slowly after birth, throughout childhood, again reaching the adult value at puberty. Serum proteins always contribute the smaller part to the total protein in the blood, but their contribution (by mass) varies from 16%

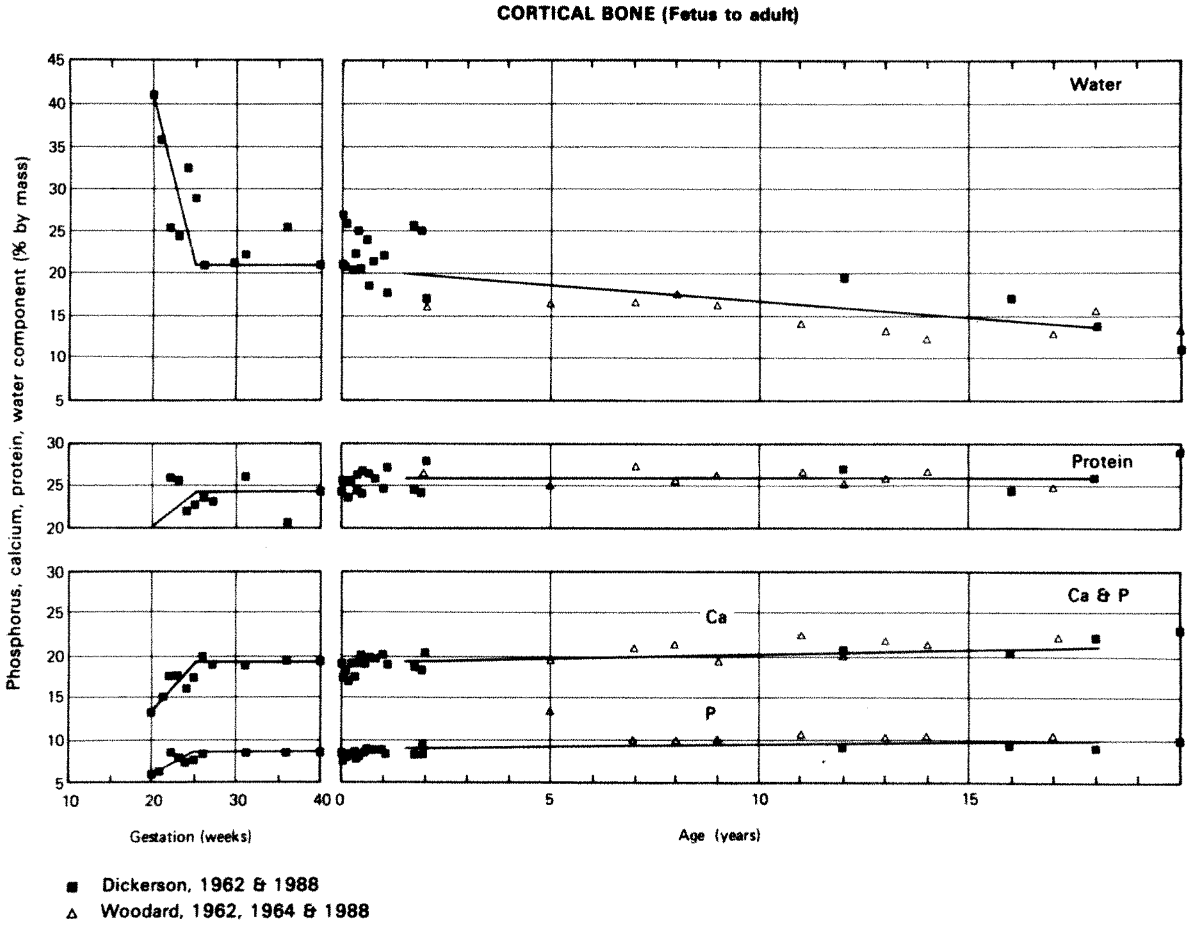

Figure 3. Plots of phosphorus, calcium, protein and water content *versus* age (20-week-old fetus to 18-year-old young adult) for cortical bone. The points at 40 weeks gestation on the 20 to 40 week graphs are also plotted on the 0 to 18 year graphs. Graphs are fitted to plotted data.

in the fetus at 11% at birth, to 22–24% at 6 months and is about 20% throughout childhood and in the adult.

Brain—whole. The brain, like most other organs, consists of distinct parts which differ in composition. Most of those studying the composition of the brain have treated these parts separately. However, for the present purpose, values for the composition of whole brain are given.

The brain grows very rapidly from mid-gestation to 18 months after birth, by which time it has reached about 70% of its adult mass. Increase in mass continues, but at a much slower rate. Growth and development of the brain are characterized by a decrease in the percentage of water and an increase in protein. Brain differs from most other tissues, however, in that lipids form an integral part of the structure. The membrances of oligodendroglial cells grow and thicken to form the myelin sheath around nerve axons and are visible in the brain as white matter. Myelination begins before birth, but most of it takes place between birth and 3 years of age, when the brain is 80–90% of its mass at maturity. Because deposition of lipids continues rapidly after the rate of growth of the brain has slowed down, there is a considerable increase in concentration of lipid between 18 months and 3 years, with consequent decrease in the percentage of water. After 3 years, the changes in composition are relatively small.

Heart. The heart is a muscular organ and, like other organs, it is not a simple structure. The composition of the atria and ventricles is different, the atria containing the most water and least protein, and the left ventricle the opposite. The values shown in Tables II and III represent whole heart muscle. The changes in composition with age are partly due to changes in the relative proportions of the different parts. Changes in composition are small between 17 weeks gestation and full-term, and adult values are reached between 2 and 4 years.

Kidney. A kidney consists of two main parts, the medulla and cortex, and the composition of the two parts is different, the medulla containing more water

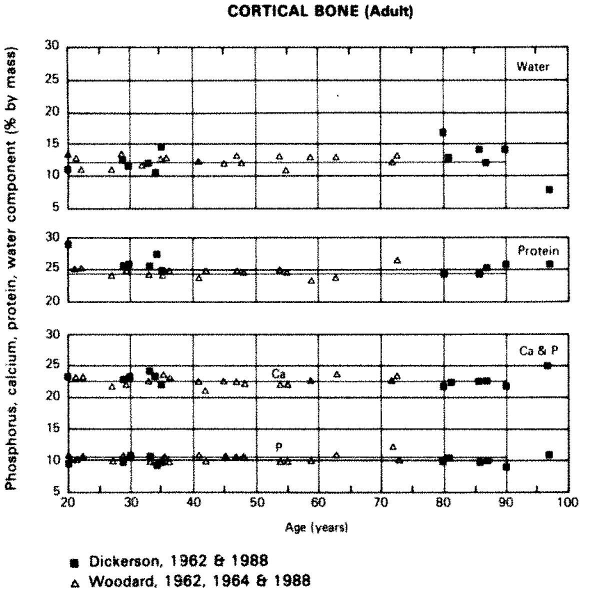

Figure 4. Plots of phosphorus, calcium, protein and water content *versus* age (20-year-old to 90-year-old adult) for cortical bone. Graphs are fitted to plotted data.

and less protein than the cortex. This is partly related to the fact that the renal tubules contain some urine in life and after death. It is important, therefore, that whole kidneys are analysed and not a slice of cortex, if it is the composition of the whole kidney that is required. The values given here apply to the kidney as a whole. The changes in composition with age are similar to those for muscle and liver. Kidney has more sodium and less potassium at each age than muscle or liver.

Liver. The changes in composition of the liver with development are in the same direction as in skeletal muscle, but over the age interval considered here they are quantitatively smaller, so that the liver of the fetus is nearer its adult composition than skeletal muscle. This may be related to function.

The liver can incorporate large quantities of lipid in certain diseases and states of malnutrition (see Discussion), but in the normal child lipid does not usually account for more than 4–5% of the mass. Carbohydrate is stored as glycogen and the amount of this varies according to the state of nutrition. It also varies with development, increasing always with the lipid content of the body during the last third of gestation and falling rapidly after birth.

Lung. The lungs after death, as in life, inevitably contain blood, and figures for composition represent lung tissues plus an unknown quantity of blood. There is very little change in the composition of lung while the fetus is in the uterus, but when the lungs expand and breathing begins the characteristic changes in composition begin to take place; a fall in the percentage of water and a consequent rise in the protein concentration. The presence of blood makes little difference to the elemental composition of the deflated organ.

Muscle—skeletal. Skeletal muscle comprises about 25% of the mass of a newborn infant (Dickerson & Widdowson, 1960) and approximately 30–40% of the mass of an adult (ICRP, 1975). It therefore forms a larger part of the body mass than any other soft tissue except in extremely obese individuals, when adipose tissue may predominate.

The characteristic change in the composition of skeletal muscle during early development is a decrease in the percentage of water and an increase in the protein concentration. As the fibres increase in number and size the extracellular material, which makes up a large part of fetal skeletal muscle, is replaced by muscle fibres. The number of muscle fibres is probably complete soon after a full-term birth, but their size continues to increase throughout growth. By 6 months after birth the changes in composition are slowing down, and for the present purpose the adult values for composition have been taken for all ages above 6 months. As in the liver, glycogen is deposited in muscle during the last third of gestation. The formation of glycogen leads to an increase in water and phosphate in the cells.

Placenta. The figures obtained by chemical analysis for the composition of the placenta depend partly upon the amount of blood left within it. The values given here are for placenta drained of blood as far as possible after delivery.

The changes in composition of the placenta during gestation are similar to those in the organs and tissues of the fetal body. Placental tissue contains very little lipid.

Skin. Much of the lipid in the human body lies beneath the dermal layer of the skin. It is impossible to remove all the underlying adipose tissue by dissection. Consequently, the values shown in Tables II and III represent skin from which all lipid has been removed by chemical means.

As in other tissues, the percentage of water falls during development, and the protein concentration increases, but there is at the same time a change in type of protein that is deposited. In the fetus, less than 20%, by mass, of the protein consists of collagen, much of the remainder being elastin; by term the percentage mass of the protein as collagen has risen to 63%, by 6 months to 70%. In adult skin, 90%, by mass, of the protein is present in this form.

Spleen. Like many other organs, the spleen is made up of several types of tissue, smooth muscle, connective tissue, lymphatic tissue and a variable amount of blood. When the spleen is removed from an adult at operation or immediately after death, the organ contracts and much of the blood in it is lost. In the newborn infant the spleen acts as a blood-forming organ rather than as a reservoir of blood. The values for spleen given here suggest a change in composition in the same direction as for other tissues. The values for adult spleen do not necessarily represent the organ filled with blood as it is in the living body (see Discussion).

Table II. Water, lipid, protein, carbohydrate and mineral components of the soft tissues

Body tissue	Percentage by mass				
	Water	Lipid	Protein	Carbohydrate	Minerals[b]
Adipose tissue[a]					
Newborn 1	71.6	22.8	5.4	—	0.2
Newborn 2	59.7	34.7	5.4	—	0.2
Newborn 3	47.8	46.6	5.4	—	0.2
Infant (2 days–10 months) 1	57.7	35.5	6.6	—	0.2
Infant (2 days–10 months) 2	47.6	47.2	5.0	—	0.2
Infant (2 days–10 months) 3	37.5	58.9	3.4	—	0.2
Child (1–18 years) 1	53.6	41.7	4.5	—	0.2
Child (1–18 years) 2	41.1	55.0	3.7	—	0.2
Child (1–18 years) 3	28.6	68.3	2.9	—	0.2
Adult 1	30.5	61.4	7.9	—	0.2
Adult 2	21.2	74.1	4.4	—	0.3
Adult 3	11.4	87.3	1.0	—	0.3
Blood—whole					
Fetus (20 weeks)	86.0	(0.5)	12.8	0.1	0.6
Newborn	75.0	(0.5)	23.8	0.1	0.6
Infant (1 week)	76.8	(0.5)	22.0	0.1	0.6
Infant (6–12 months)	82.5	(0.5)	16.3	0.1	0.6
Adult	79.0	0.6	19.6	0.1	0.7
Brain—whole[c]					
Fetus (14 weeks)	93.2	1.5	3.8	0.6	0.9
Newborn	89.6	2.6	6.2	0.8	0.8
Infant (18 months)	83.9	6.1	8.2	(1)	0.8
Child (3–18 years)			As adult		
Adult	75.5	11.6	10.7	1.0	1.2
Heart					
Fetus (17–40 weeks)	85.9	1.8	10.5	1.1	0.7
Child (2 years)	83.9	2.5	12.9	—	0.7
Child (4–18 years)	81.3	3.4	14.5	—	0.8
Adult	75.9	6.2	17.1	—	0.8
Kidney					
Fetus (17–40 weeks)	88.1	1.9	9.2	—	0.8
Child (2 years)	83.3	3.6	12.3	—	0.8
Child (4–18 years)			As adult		
Adult	76.6	4.8	17.7	—	0.9
Liver					
Fetus (17–40 weeks)	83.0	2.4	12.1	1.7	0.8
Child (1 year)	77.0	4.1	16.0	(2)	0.9
Child (4–18 years)			As adult		
Adult	74.5	4.6	17.6	2.2	1.1
Lung					
Fetus (17–40 weeks)	85.7	1.8	10.3	1.5	0.7
Adult	80.6	1.3	17.1	—	1.0
Muscle—skeletal					
Fetus (15 weeks)	90.4	0.9	7.9	—	0.8
Newborn	80.6	2.0	14.0	2.8	0.6
Infant (3 months)	79.2	2.0	17.2	1.0	0.6
Infant/child (6 months–18 years)		As adult, but with lipid content increasing from 2.1–4.2			
Adult	74.1	4.2	19.8	1.0	0.9
Placenta					
17–26 weeks	88.0	1.3	10.1	—	0.6
Above 26 weeks	83.1	1.2	15.1	—	0.6

Table II cont.

Body tissue	Percentage by mass				
	Water	Lipid	Protein	Carbohydrate	Minerals[b]
Skin (lipid-free)					
Fetus (14 weeks)	92.0	—	7.3	—	0.7
Newborn	82.7	—	16.6	—	0.7
Adult	72.1	—	27.2	—	0.7
Spleen					
Fetus (26–40 weeks)	83.8	1.5	13.9	—	0.8
Adult	78.7	1.8	18.6	—	0.9

Data for adult extracted from Woodard and White (1986).

[a] For adipose tissue the numbers 1, 2 and 3 refer to compositions based on the mean (M) and standard deviation (σ) of each component (water, lipid and protein) and correspond to $M-\sigma$, M and $M+\sigma$.

[b] Includes remaining elements with $Z > 8$.

[c] Lipid in brain assumed to be 50% sphingomyelin + 25% cerebroside + 25% cholesterol, by mass. The lipid content for the adult is the average of the values for white and grey matter.

Table III. The elemental compositions of the soft tissues

Body tissue	Elemental composition (% by mass)										Densities		
											Mass	Electron	
	H	C	N	O	Na	P	S	Cl	K	Others	kg m^{-3}	el kg^{-1} $\times 10^{26}$	el m^{-3} $\times 10^{26}$
Adipose tissue[a]													
Newborn 1	11.1	20.5	0.9	67.2	0.1		0.1	0.1			1000	3.339	3339
Newborn 2	11.1	29.7	0.9	58.0	0.1		0.1	0.1			990	3.339	3306
Newborn 3	11.2	39.0	0.9	48.6	0.1		0.1	0.1			980	3.342	3275
Infant (2 days–10 months) 1	11.1	31.0	1.1	56.5	0.1		0.1	0.1			990	3.339	3306
Infant (2 days–10 months) 2	11.2	39.2	0.9	48.4	0.1		0.1	0.1			970	3.342	3241
Infant (2 days–10 months) 3	11.4	47.3	0.6	40.4	0.1		0.1	0.1			960	3.347	3213
Child (1–18 years) 1	11.2	34.7	0.8	53.0	0.1		0.1	0.1			980	3.342	3275
Child (1–18 years) 2	11.3	44.5	0.6	43.3	0.1		0.1	0.1			960	3.344	3211
Child (1–18 years) 3	11.5	54.3	0.5	33.4	0.1		0.1	0.1			950	3.350	3183
Adult 1	11.2	51.7	1.3	35.5	0.1		0.1	0.1			970	3.342	3241
Adult 2	11.4	59.8	0.7	27.8	0.1		0.1	0.1			950	3.347	3180
Adult 3	11.6	68.1	0.2	19.8	0.1		0.1	0.1			930	3.353	3118
Blood—whole													
Fetus (20 weeks)	10.5	7.3	2.2	79.2	0.1	0.1	0.1	0.2	0.2	Fe (0.1)	1040	3.321	3454
Newborn	10.0	13.1	4.0	72.0	0.1	0.1	0.2	0.2	0.2	Fe (0.1)	1070	3.306	3538
Infant (1 week)	10.1	12.2	3.7	73.1	0.1	0.1	0.2	0.2	0.2	Fe (0.1)	1070	3.309	3541
Infant (6–12 months)	10.4	9.1	2.8	76.8	0.1	0.1	0.2	0.2	0.2	Fe (0.1)	1050	3.318	3484
Adult	10.2	11.0	3.3	74.5	0.1	0.1	0.2	0.3	0.2	Fe (0.1)	1060	3.312	3511
Brain—whole													
Fetus (14 weeks)	10.9	3.3	0.7	84.2	0.2	0.2		0.3	0.2		1020	3.333	3400
Newborn	10.8	5.5	1.1	81.6	0.2	0.3	0.1	0.2	0.2		1030	3.330	3430
Infant (18 months)	10.7	9.1	1.6	77.6	0.2	0.3	0.1	0.2	0.2		1030	3.327	3427
Adult	10.7	14.5	2.2	71.2	0.2	0.4	0.2	0.3	0.3		1040	3.327	3460
Heart													
Fetus (17–40 weeks)	10.6	7.5	1.8	79.3	0.2	0.1	0.1	0.2	0.2		1040	3.324	3457
Child (2 years)	10.5	8.8	2.2	77.7	0.1	0.2	0.1	0.2	0.2		1040	3.321	3454
Child (4–18 years)	10.5	10.4	2.5	75.7	0.1	0.2	0.1	0.2	0.3		1040	3.321	3454
Adult	10.4	13.9	2.9	71.8	0.1	0.2	0.2	0.2	0.3		1050	3.318	3484

Table III cont.

Body tissue	Elemental composition (% by mass)										Densities		
											Mass	Electron	
	H	C	N	O	Na	P	S	Cl	K	Others	kg m^{-3}	el kg^{-1} $\times 10^{26}$	el m^{-3} $\times 10^{26}$
Kidney													
Fetus (17–40 weeks)	10.7	6.4	1.6	80.4	0.2	0.2	0.1	0.2	0.2		1030	3.327	3427
Child (2 years)	10.6	9.4	2.1	77.0	0.2	0.2	0.1	0.2	0.2		1040	3.324	3457
Adult	10.3	13.2	3.0	72.4	0.2	0.2	0.2	0.2	0.2	Ca (0.1)	1050	3.315	3481
Liver													
Fetus (17–40 weeks)	10.5	9.1	2.1	77.4	0.2	0.2	0.1	0.2	0.2		1040	3.321	3454
Child (1 year)	10.3	12.6	2.7	73.3	0.1	0.3	0.2	0.2	0.3		1050	3.315	3481
Adult	10.2	13.9	3.0	71.6	0.2	0.3	0.3	0.2	0.3		1060	3.312	3511
Lung													
Fetus (17–40 weeks)	10.6	7.6	1.8	79.2	0.2	0.2	0.1	0.2	0.1		1040	3.324	3457
Adult	10.3	10.1	2.9	75.5	0.2	0.2	0.3	0.3	0.2		1050	3.315	3481
Muscle—skeletal													
Fetus (15 weeks)	10.8	4.9	1.3	82.1	0.2	0.1	0.1	0.3	0.2		1030	3.330	3430
Newborn	10.4	10.3	2.4	76.2	0.1	0.1	0.1	0.2	0.2		1050	3.318	3484
Infant (3 months)	10.3	11.2	2.9	74.8	0.1	0.1	0.2	0.2	0.2		1050	3.315	3481
Adult	10.2	14.3	3.4	71.0	0.1	0.2	0.3	0.1	0.4		1050	3.312	3478
Placenta													
17–26 weeks	10.7	6.4	1.7	80.5	0.2	0.1	0.1	0.2	0.1		1030	3.327	3427
Above 26 weeks	10.4	9.0	2.6	77.2	0.2	0.1	0.2	0.2	0.1		1040	3.318	3451
Skin (lipid-free)													
Fetus (14 weeks)	10.8	3.9	1.2	83.3	0.2	0.1	0.1	0.3	0.1		1020	3.330	3397
Newborn	10.4	8.9	2.8	77.0	0.2	0.1	0.2	0.3	0.1		1050	3.318	3484
Adult	9.9	14.5	4.6	70.0	0.2	0.1	0.3	0.3	0.1		1110[b]	3.303	3667
Spleen													
Fetus (26–40 weeks)	10.5	8.6	2.4	77.6	0.2	0.2	0.1	0.2	0.2		1040	3.321	3454
Adult	10.3	11.3	3.2	74.1	0.1	0.3	0.2	0.2	0.3		1060	3.315	3514

[a] See footnote Table II.

[b] Estimated from measured values quoted in Woodard and White (1986).

Table IV. Water, lipid, protein, carbohydrate and mineral components of cortical bone

Body tissue	Percentage by mass				
	Water	Lipid	Protein	Carbohydrate	Minerals[b]
Fetus (20 weeks)	41.2	—	20.4	(5)	33.4
Fetus (23 weeks)	29.5	—	22.7	(5)	42.8
Newborn	21.1	—	24.3	(5)	49.6
Infant (3 months)	23.2	—	24.8	(5)	47.0
Child (1 year)	20.7	—	26.1	(5)	48.2
Child (5 years)	18.9	—	25.8	(5)	50.3
Child (10 years)	16.9	—	25.8	(5)	52.3
Child (15 years)	15.0	—	25.8	(5)	54.2
Adult[a]	12.2	—	24.6	5.2	58.0

[a] From Woodard and White (1986).

[b] Includes remaining elements with $Z > 8$.

Table V. The elemental compositions of cortical bone

Body tissue	Elemental composition (% by mass)										Densities		
											Mass	Electron	
	H	C	N	O	Na	Mg	P	S	Cl	Ca	kg m^{-3}	el kg^{-1} $\times 10^{26}$	el m^{-3} $\times 10^2$
Fetus (20 weeks)	6.4	12.8	3.5	57.1	0.1	0.1	6.1	0.2	0.2	13.5	1430	3.193	4566
Fetus (23 weeks)	5.2	14.3	3.9	51.7	0.1	0.1	7.7	0.2	0.1	16.7	1580	3.156	4987
Newborn	4.4	15.3	4.1	47.7	0.1	0.2	8.5	0.2	0.1	19.4	1720	3.131	5386
Infant (3 months)	4.7	15.4	4.2	48.5	0.1	0.2	8.2	0.2	0.1	18.4	1680	3.141	5276
Child (1 year)	4.5	15.9	4.4	46.7	0.1	0.2	8.7	0.3	0.1	19.1	1710	3.134	5359
Child (5 years)	4.3	15.8	4.4	45.7	0.1	0.2	9.3	0.3	0.1	19.8	1750	3.128	5473
Child (10 years)	4.0	15.9	4.4	45.0	0.1	0.2	9.6	0.3	0.1	20.4	1790	3.118	5582
Child (15 years)	3.8	16.0	4.4	44.3	0.1	0.2	9.9	0.3		21.0	1830	3.112	5696
Adult	3.4	15.5	4.2	43.5	0.1	0.2	10.3	0.3		22.5	1920	3.100	5952

Skeletal tissues

Cortical bone. The proportion of water in cortical bone falls from 41% to 21%, by mass, between 20 and 25 weeks gestation (Fig. 3). The subsequent fall to 14%, by mass, at 18 years occurs gradually. The early fall in the proportion of water is accompanied by sharp rises in the concentrations of protein, calcium and phosphorus. The values of these components at different ages are shown in Table IV. They suggest that during the first 3 months after birth the proportion of water in cortical bone rises and that of minerals falls. Adult values for all these constituents are reached by 18–20 years of age, with the composition remaining essentially constant through to 90 years (Fig. 4).

Discussion

One problem in the analysis of soft tissues is the presence of blood. This has been referred to already in respect of lungs, spleen and placenta. In life all organs and tissues contain blood, but after death blood begins to diffuse out of the tissues, and the mode of death makes a considerable difference to the amount that is lost. If there has been much bleeding, for example because of an accident, extracellular fluid will be lost, not only from the circulation, but from tissues as well. Skeletal muscle, for example, appears to have a different chemical composition according to whether the individual has bled or not bled before death. This applies particularly to the principal minerals in extracellular fluid, sodium and chloride ions (Widdowson & Southgate, 1959).

The tendency among tissue analysts is to remove as much as possible of the remaining blood in the dead tissue before analysis. Thus, in the soft tissues described in Tables II and III, all blood clots were removed from the hearts, but not blood within the heart muscle. Some, but not all, blood was removed from lungs, spleen and placenta, while livers and kidneys were blotted free of surface blood. Some blood remained in skeletal muscle, less in adipose tissue and skin. The compositions of whole blood of the immature fetus, newborn infant and adult are given in Tables II and III, and may be used to investigate the effects of additional blood content on specific soft tissue compositions.

In this study the composition of lipid-free skin was assessed. Difficulties in dissecting skin specimens without subcutaneous adipose tissue adhering to them are probably the major cause of the variability of reported lipid contents in skin.

The major part of the skeletons of most adult mammals consist of articulated rigid mineralized structures each of which may or may not enclose the unrelated bone marrow. The rigid material or "osseous tissue" is commonly referred to as "cortical bone". This kind of bone is the substance of the cortex and the trabeculae, the millimetre-sized bony sheets which gave rigidity to the spongiosa. In the adult, the chemical

Table VI. Contribution of organs and tissues to total body mass at different ages (from Widdowson & Dickerson, 1964; ICRP, 1975; White et al, 1987)

Body tissue	Percentage of total body mass			
	Fetus (20–24 weeks)	Newborn baby	Adult	
			Male	Female
Adipose tissue	–	–	17.9	29.3
Blood—whole	–	[b]	5.3	5.3
Brain—whole	13.0	13.0	2.0	2.1
Heart	0.6	0.5	0.5	0.4
Kidneys (2)	3.1	1.6	0.4	0.5
Liver	4.0	5.0	2.6	2.4
Lungs (2)	–	–	1.4	1.4
Muscle—skeletal	25.0	25.0	40.0	29.3
Skin	13.0	15.0	3.7	3.1
Spleen	–	0.2	0.3	0.3
Skeleton—whole[a]	22.0	18.0	17.1	17.1

[a] Includes osseous tissue, marrow and cartilage.

[b] 7.7 ml per kg body mass.

composition of cortical and trabecular bone is almost identical (Arnold, 1960).

Up to about 10 weeks gestation the human skeleton is composed entirely of cartilage, a tissue quite distinct histologically and chemically from cortical bone. Its composition in the adult is (by mass) water, 75%; protein, 11%; chondroitin sulphate, 11%; mineral, 3% (Woodard & White, 1986). At about 10 weeks a primary centre of ossification begins to develop in the shafts of long bones, like the femur, and the collagen laid down is calcified by the deposition in it of mineral which is similar to the terrestrial mineral, hydroxyapatite. The osseous tissue gradually extends along the shaft, replacing the cartilage and forming also the spongy trabecular bone of the metaphyses. The bone formed during fetal life is described as "woven" bone. This bone disappears as the bones grow as a result of remodelling. Prior to the formation of the primary centre of ossification, the degree of calcification, measured by the calcium/nitrogen (Ca/N) ratio, may be assumed to be almost zero but has risen to about 3 by 12–14 weeks gestation, about 5 by full-term and about 6 by 18–35 years (Dickerson, 1962).

The change in the calcification of osseous tissue during growth depends on the availability of mineral. Table IV shows that there is a tendency for the concentration of mineral in the femoral cortex to fall after birth and then to begin to rise again by 1 year. These changes are more evident in metaphyseal spongy bone (Dickerson, 1962) and particularly in the bones of faster growing species like the kitten (Slater & Widdowson, 1962). It was shown that the fall in the Ca/N ratio could be prevented by giving calcium phosphate supplements to suckling kittens.

The organs and tissues of the body grow and mature at different rates so that the adult body is formed by a differential process. Thus, at a given age during growth the composition of the body is the result of the contribution to the total body mass of the individual organs and tissues and of their composition at that age. Both organ/tissue mass and tissue composition change during development. Table VI shows the contribution of organs and tissues to the body mass in a typical healthy fetus, newborn infant and adult (male and female). At each age, skeletal muscle, skin, skeleton, liver and brain account for more than 70% of the body mass. Skeletal muscle and brain contribute the same proportion of the mass in the fetus and newborn infant. In the adult (male and female) the proportion contributed by skeletal muscle is much higher while that contributed by the brain is much lower than in the infant. The proportion of the body mass contributed by skeleton is similar in the adult as it is at birth and at both ages is a little less than in the fetus. The ratio of adipose to skeletal muscle in the adult male is considerably lower than in the adult female.

The composition and mass of body tissues may be markedly affected by both overnutrition and undernutrition. The main effect of overnutrition is on adipose tissue. The total quantity of lipid in adipose tissue in the body increases, both in the subcutaneous and deep body sites, and the adipocytes become filled with lipid and may increase in number. The proportion of lipid in the tissue increases and that of water decreases as the space between the cells diminishes (Garrow, 1974). The extent of these changes depends on the degree of overnutrition and obesity. Fatty infiltration of the liver can also occur, but that is more likely to be caused by an excessive intake of alcohol than energy.

The changes resulting from undernutrition cause a change in the contribution of the organs and tissues to the total body mass. The brain and skeleton which are affected least by undernutrition come to contribute more to the body mass whilst muscle and adipose tissue contribute less. Undernutrition of differing severity is common in hospital patients and tends to be progressive, the severity increasing with their length of stay (Hill et al, 1977). Patients in hospital may become almost literally "skin and bone".

Quantitative data on the composition of abnormal body tissues because of disease and changes in nutrition will be the subject of a future publication.

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Technical note

Defaecography commode with ruler mounted on the side: reference point for measurements of perineal descent

By Michael Bachmann Nielsen, MD

Department of Diagnostic Radiology, Glostrup Hospital, University of Copenhagen, DK 2600 Glostrup, Copenhagen, Denmark

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Videodefaecography is performed in our department according to the technique previously described by Skomorowska et al (1987, 1988). The procedure (Mahieu et al, 1984) can be simplified further by placing a ruler with lead markings on the side of the commode (Bernier et al, 1988). All measurements can then be made from videotape, and static images are not needed.

Approximately 300 ml of thick barium contrast medium (a mixture of half volume Mixobar oesophagus® and half volume Mixobar suspension®) is instilled into the rectosigmoid colon through a catheter which is then removed. The patient is placed on the commode in front of a fluoroscopic unit. A ruler, with lead markings at intervals of 1 cm, is glued on the side of the chair closest to the film (Fig. 1).

During fluoroscopy, lateral views of the rectum and anal canal are obtained and registered on video tape at all stages of defaecation. No static images are taken. The fluoroscopic position is not usually changed during the procedure. However, in cases where it has to be changed, the lead markers serve as a reference point, allowing measurement of the degree of perineal descent directly during the examination or from the video sequence (Fig. 2).

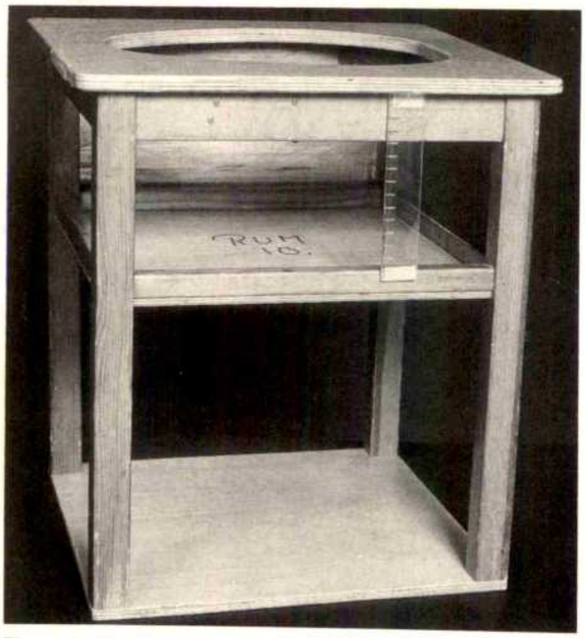

Figure 1. The defaecography commode with the ruler on the side.

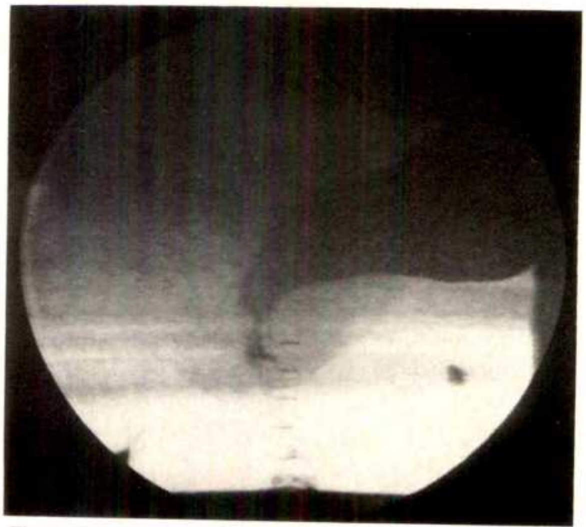

Figure 2. Lateral projection of the rectum at rest. The ruler is visible in the bottom of the picture.

From the video sequence, the anorectal angle can be measured by freezing the images taken at rest and during maximum strain. Static radiographs are not needed as all measurements can be made from the videorecording.

As the commode is in a fixed position between the X-ray source and the film, the magnification factor remains constant. The unit used here had a magnification factor of 1·26 : 1 as measured from the ruler.

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Case reports

Prenatal diagnosis of unilateral renal disease in tuberous sclerosis

By *J. Blethyn, MB, ChB, FRCR, †A. Jones, MB, BCh, FRCR and †B. Sullivan, MB, BCh, FRCR

*Department of Radiology, University Hospital of Wales, Cardiff, UK and †Department of Radiology, Royal Gwent Hospital, Newport, UK

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Keywords: Renal disease, Tuberous sclerosis, Prenatal diagnosis

Sonographic demonstration of an abnormal kidney as the presenting feature of tuberous sclerosis has not been described previously. A large echogenic kidney was first shown on routine prenatal 28 week ultrasound and confirmed as cystic on biopsy after birth. Generalized convulsions and depigmentation developed in infancy and CT showed cerebral cortical tubers.

Case report

An enlarged echogenic left kidney was discovered on routine antenatal sonography of a 28 week fetus in a 27-year-old gravida 1 mother (see Figs 1 and 2). The previous 16 week ultrasound scan was normal. A provisional diagnosis of multicystic dysplastic kidney was made in view of the normal right kidney and bladder. A detailed fetal ultrasound at 32 weeks confirmed the unusual appearance of the left kidney, but did not detect any abnormality in the contralateral kidney, the head or the heart. After an uncomplicated term delivery an early neonatal scan confirmed an enlarged "hyperechoic" left kidney (Fig. 3). The right kidney was normal. An isotope renogram shortly afterwards showed only 10% excretion on the abnormal side. This was thought at that time to be more likely to be an adult type polycystic kidney or a hamartomatous lesion because of the unilateral nature of the lesion.

At 5 weeks of age the baby had minor convulsions and EEG changes suggesting a right frontal focus. Cranial sonography (Figs 4 and 5) demonstrated an echogenic area in the right frontal cortex with no acoustic shadowing. Computed tomography confirmed this lesion to be of high attenuation (Fig. 6). Two other high attenuation masses were shown in the temporo-parietal cortex which all enhanced slightly with intravenous contrast medium. The initial diagnosis was revised and tuberous sclerosis was considered to be the likely cause of the cerebral and renal lesions. Brain CT was repeated at 2 months and revealed curvilinear calcification within the cortical tubers.

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* Author for correspondence.

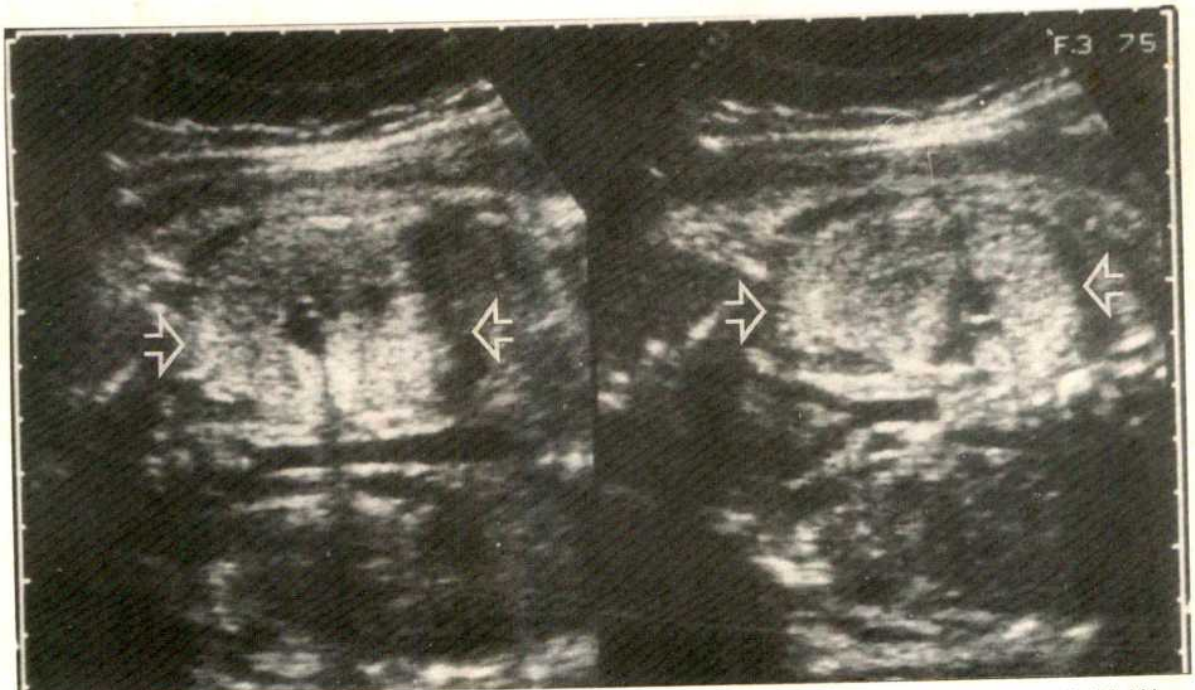


Figure 1. Antenatal ultrasound at 28 weeks gestation shows a longitudinal section through an enlarged echogenic left kidney measuring 5.5 cm in diameter and a normal right kidney. The inferior vena cava is seen separating the kidneys. Arrows show the outlines of the left kidney.

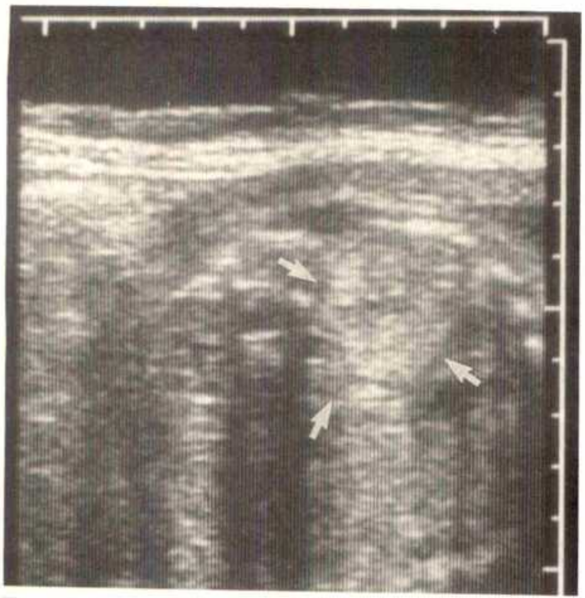
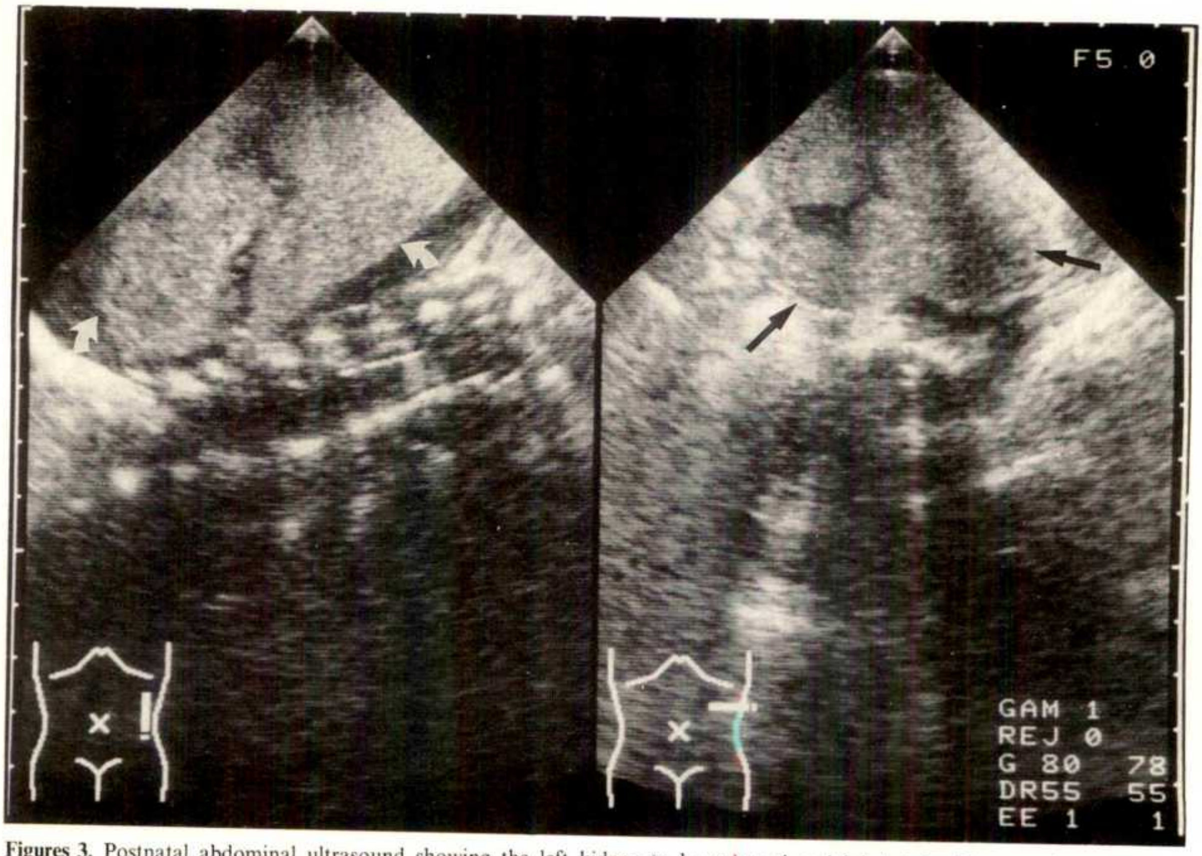


Figure 2. Antenatal ultrasound at 29 weeks gestation shows a transverse section at the level of the hilum through an enlarged echogenic left kidney. Arrows show the outlines of the kidney.

Depigmented macules appeared on the infant's legs which failed to fluoresce under Wood's Light but were compatible with a diagnosis of tuberous sclerosis. Abdominal CT (Fig. 7) showed the left kidney to be lobulated with a heterogeneous, partly cystic structure but no fat density. Renal biopsy at this time confirmed microscopic cysts, and a list of differential diagnoses, including tuberous sclerosis, was given. Clinical examination of the eyes and heart showed no abnormality and there was no family history of tuberous sclerosis.

Discussion

Of the differential diagnoses, one considered was the Laurence–Moon–Biedl syndrome with cystic nephropathy, pigmented retinopathy, polydactyly, obesity, genital hypoplasia and mental retardation. The kidneys are usually small with fetal lobulation, cystic dysplasia and clubbed calyces. Abnormal kidneys are described in the Beckwith–Wiedemann syndrome as being enlarged with smooth margins, diffusely increased echogenicity and normal or enlarged calyces. The other features of a large tongue, omphalocele and hepatomegaly were not present in this child (Taybi, 1983). Mesoblastic nephroma and Wilms' tumour can have an identical appearance ranging from predominantly solid to cystic. Renal cortical cysts and seizures occur in cerebrohepatorenal syndrome in conjunction with craniofacial dysmor-



Figures 3. Postnatal abdominal ultrasound showing the left kidney to be enlarged and lobulated with a varying pattern of echogenicity. There is no corticomedullary differentiation and there are no visible cysts. Arrows show the margins of the right kidney in longitudinal and transverse section.

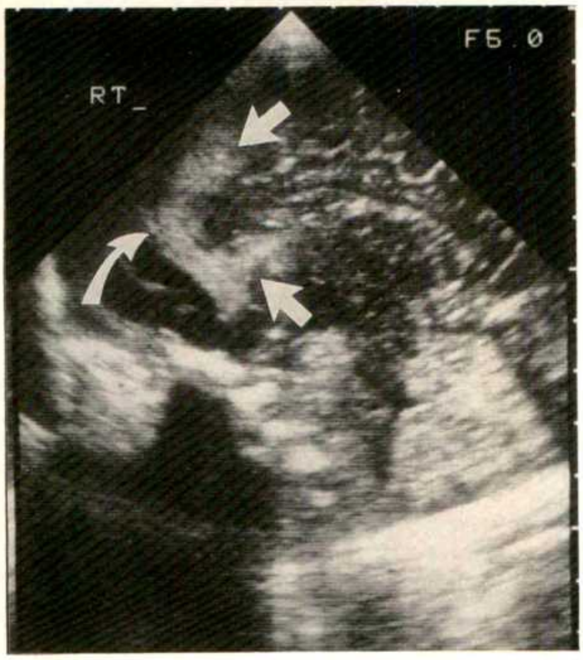


Figure 4. Cranial ultrasound at 5 weeks of age. Sagittal sections show an echogenic crescentic structure in the right frontal area (arrowed).

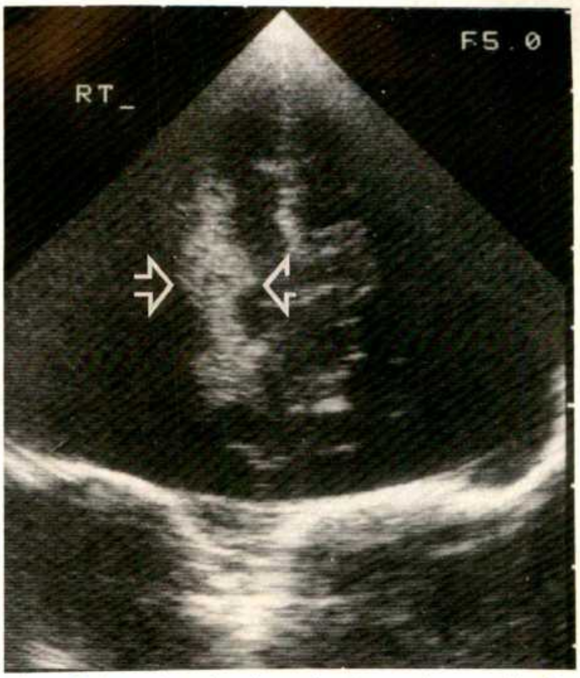
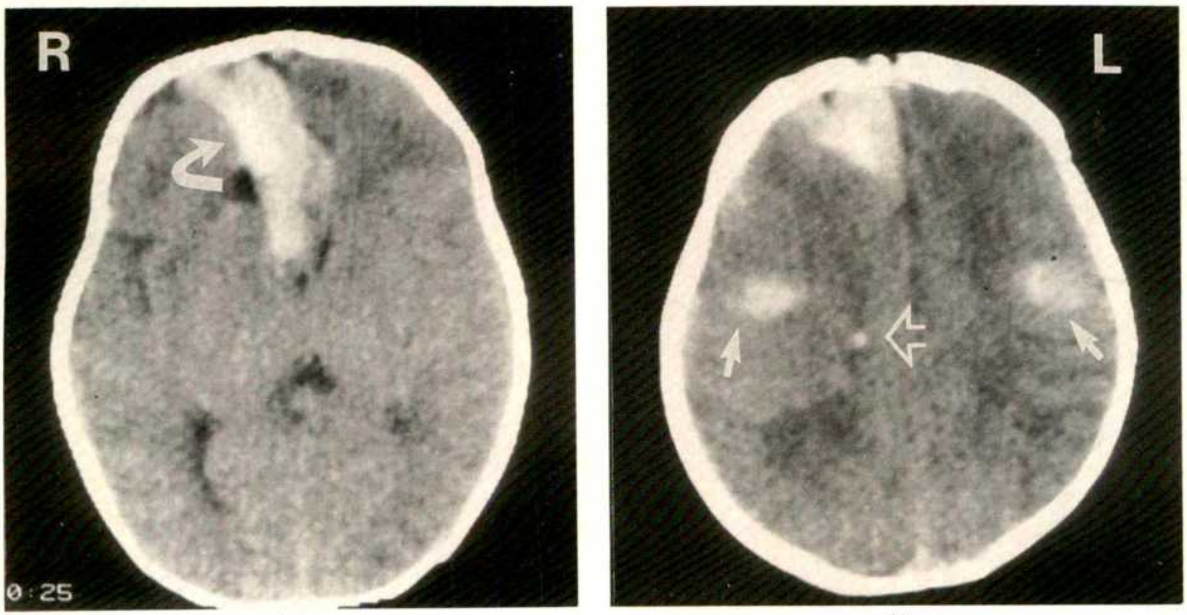


Figure 5. Coronal section shows the abnormal area outlined by arrows.

phism, hepatomegaly, skeletal abnormalities and hypotonia (Taybi, 1983). Calcified cortical tubers in the brain are a characteristic finding in tuberous sclerosis not occurring in any of these conditions described above.

We can find no previous reference in the literature to prenatal detection of a renal abnormality in tuberous sclerosis. Intracardiac and intracranial tumours have been detected by prenatal sonography but the kidneys



(a) (b)

Figure 6. Unenhanced brain CT at 5 weeks of age confirmed the presence of a high attenuation area in the right frontal cortex (a) and two similar areas in the parietal cortex (b) (arrows). There is a small calcified subependymal tuber in the wall of the right lateral ventricle (open arrow).

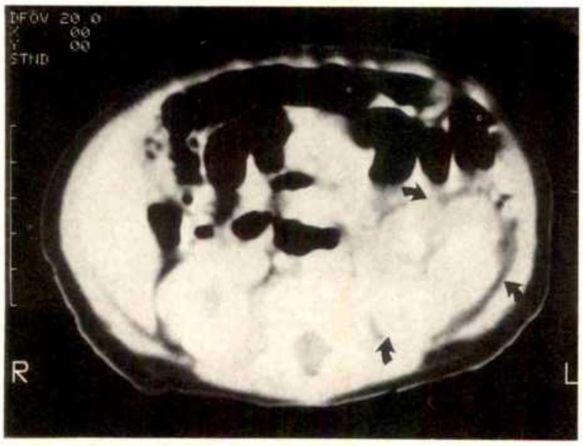


Figure 7. Abdominal CT scan at 3 months of age with intravenous contrast medium demonstrates the lobulated margins of the enlarged left kidney with a patchy nephrogram.

were normal in these cases (Journel et al, 1986; Muller et al, 1986).

Renal lesions are common in tuberous sclerosis, occurring in 54–100% of patients and consisting of angiomyolipoma (47–73%), renal cysts (18–53%) or both (12–27%) (Stillwell et al, 1987). These lesions are usually multiple, bilateral and often asymptomatic, particularly in children. Complications such as bleeding or uraemia tend to occur after 10 years of age and there is an increased incidence of renal cell carcinoma at a young age (Bernstein et al, 1986).

Renal abnormalities have been described from the age of 2 months and may be the only feature of tuberous sclerosis (Farrow et al, 1968; Stapleton et al, 1980). Pathological examination of the kidneys reveals cystic change varying from microscopic to several centimetres in diameter identical to those of infantile or adult polycystic disease, although a characteristic hyperplastic cyst epithelium has been described in these kidneys (Stapleton et al, 1980). Renal failure may occur from bleeding or compression of normal parenchyma by the enlarging cysts (Stillwell et al, 1987).

The diagnosis of tuberous sclerosis is commonly made with the onset of fits (96%) or skin lesions (73%). Some cases are completely asymptomatic but there is a significant association with mental retardation (46%) (Altman et al, 1988). Intracranial abnormalities have been described using CT and MRI (Altman et al, 1988, McMurdo et al, 1987, Sugita et al, 1985) and characteristic features include subependymal nodules, cortical tubers or haemartomas, dilated ventricles and glial tumours, with distorted cortical architecture on MRI.

Subependymal nodules are a specific finding for tuberous sclerosis and are well shown on MRI and CT. If calcification is present CT is probably more sensitive in detecting these lesions (Altman et al, 1988), but 62% of tubers shown on CT are of low attenuation. Cortical tubers may be sited anywhere in the hemisphere and can migrate into white matter (Legge et al, 1984).

There are several descriptions of atypical appearances in neonates and infants with tuberous sclerosis. Altman et al (1988) report a neonate with an atypical cerebral tuber of increased attentuation on CT and low signal intensity on MRI. Legge et al (1984) described two infants with hyperdense cortical tubers on CT but in only one case was an echogenic area seen on ultrasound. Both children had subependymal nodules on cranial sonography. A report by Frank et al (1984) describes the detection of subependymal nodules by cranial sonography in a 6-week-old infant, although cranial CT was normal. The typical changes of cortical tubers did not appear until 32 months.

In conclusion, tuberous sclerosis is a multisystem disorder which usually presents in infancy with fits; examination may reveal abnormalities of skin, kidneys, lungs or eyes. Prenatal cardiac muscle and intracranial abnormalities have been described previously and although tuberous sclerosis is an uncommon disorder it should enter into the differential diagnosis of a unilaterally enlarged echogenic kidney in the fetus.

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Gallium scintigraphy in the diagnosis and management of multifocal Castleman's disease

By *G. Stansby, FRCS, †A. Hilson, FRCP and G. Hamilton, FRCS

Academic Department of Surgery and †Department of Nuclear Medicine, Royal Free Hospital and School of Medicine, Hampstead, London NW3 2QG, UK

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Keywords: Castleman's disease, Gallium scintigraphy

Castleman's disease is a rare condition which can mimic the presentation of more common disorders. We describe the first reported case of the use of gallium scintigraphy in the multifocal form of this disease and suggest that gallium scintigraphy may have an important role to play in both its diagnosis and management.

Case report

The patient was a 37-year-old roofer who had previously always been fit and well. He was transferred to our hospital with a 10-day history of dry cough, myalgia and rigours. Except for symmetrical lower limb weakness, examination was normal and the erythrocyte sedimentation rate (ESR) was raised at 58 mm/h. The initial diagnosis was one of a post-viral myositis and he was discharged home on a reducing dose of steroids. Within a week he required readmission with low back and pleuritic left chest pain. Numerous investigations were normal including myelogram, chest radiograph, bone scan, ventilation-perfusion lung scan and a coeliac axis angiogram. His ESR had risen to 104 mm/h and his white blood cell count was elevated at 16.9×10^9 per litre. A wide range of other blood tests were normal as were creatinine clearance and urine microscopy.

While in hospital he developed a swollen left leg and a venogram revealed a left iliac vein thrombosis. A computed tomographic (CT) scan was performed which showed a small retro-psoas mass on the left side of the pelvis occluding the iliac vein (Fig. 1). Computed tomography guided biopsies revealed only necrotic tissue. A gallium scan was then performed using 122 MBq gallium citrate which showed intense uptake in this region in the left pelvis at 48 hours (Fig. 2). At this stage it was thought that the lesion was likely to be either infective or malignant.

Two further needle biopsies failed to produce a specific diagnosis either on histology or culture and when the patient failed to improve despite a trial course of antituberculous chemotherapy a laparotomy was performed. Multiple fibrinous adhesions were found throughout the abdomen but all the organs were normal. When the sigmoid colon was mobilized, a solid mass was found closely related to the ureter and iliac vessels on the left lateral wall of the pelvis; this was biopsied and the abdomen closed. Subsequently histology revealed appearances suggestive of the plasma cell variant of Castleman's disease and, 1 week following the first laparotomy, the abdomen was re-explored and the mass totally excised. The

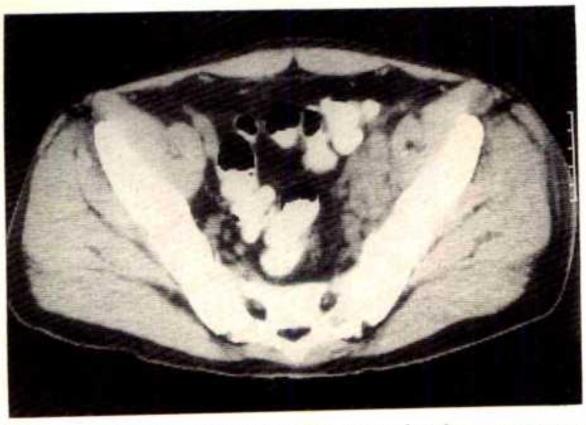

Figure 1. Computed tomographic scan showing retro-psoas mass on left.

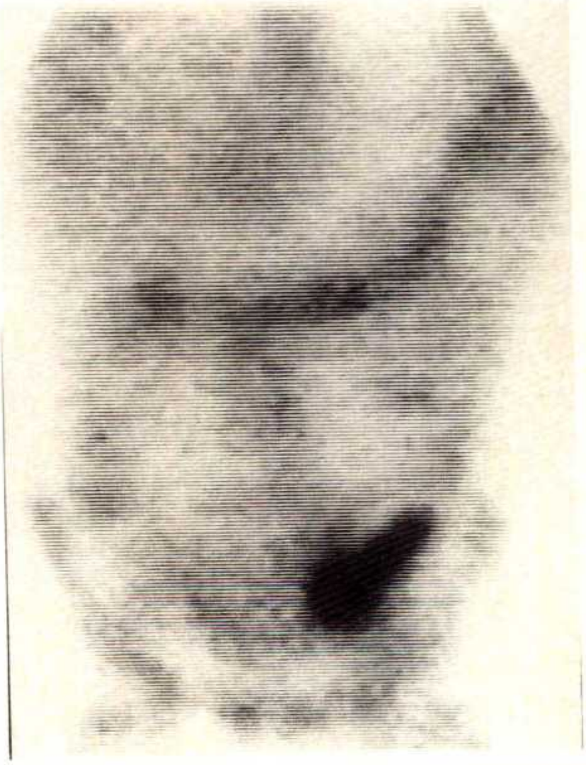

Figure 2. Gallium scintigram showing intense uptake in left side of pelvis at 48 hours.

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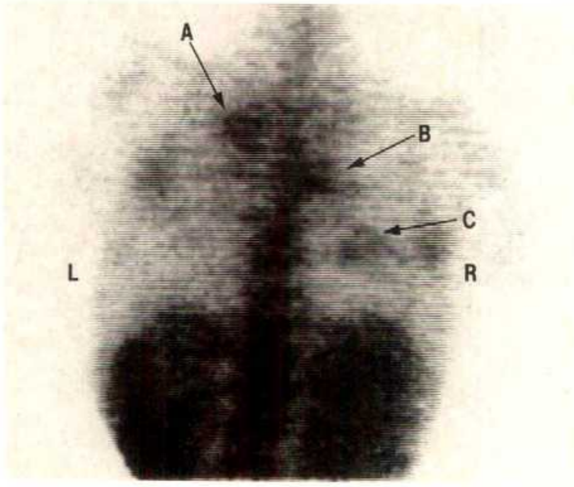

Figure 3. Gallium scintigram (posterior orientation) showing abnormal uptake in left upper zone (A), mediastinum (B) and right lower zone (C).

histology of this mass confirmed Castleman's disease and immunological studies showed no evidence of monoclonality.

After surgery he initially made a very good recovery and was discharged after 6 days on no medication. However, on review in clinic he was unwell with dyspnoea on exertion and pleuritic chest pain, and his ESR was still raised at 98 mm/h. A repeat ventilation-perfusion lung scan showed no evidence of a pulmonary embolus and a repeat gallium scintigraphy now showed no uptake in the left hemipelvis, but there was abnormal uptake in the left mediastinum as well as in the left mid zone and right lower zone (Fig. 3). Computed tomographic scan of the thorax confirmed multiple nodules within both lungs (Fig. 4) which had not been present previously. No enlarged mediastinal nodes were identified. It was felt that he was suffering from the multifocal form of Castleman's disease, and he was therefore started on azathioprine, prednisolone and indomethacin. Subsequently he improved markedly and his ESR returned to normal over a period of 6 months.. When he had clinically recovered, repeat gallium scintigraphy showed only slight uptake of tracer in the lungs and resolution of the lesions previously seen.

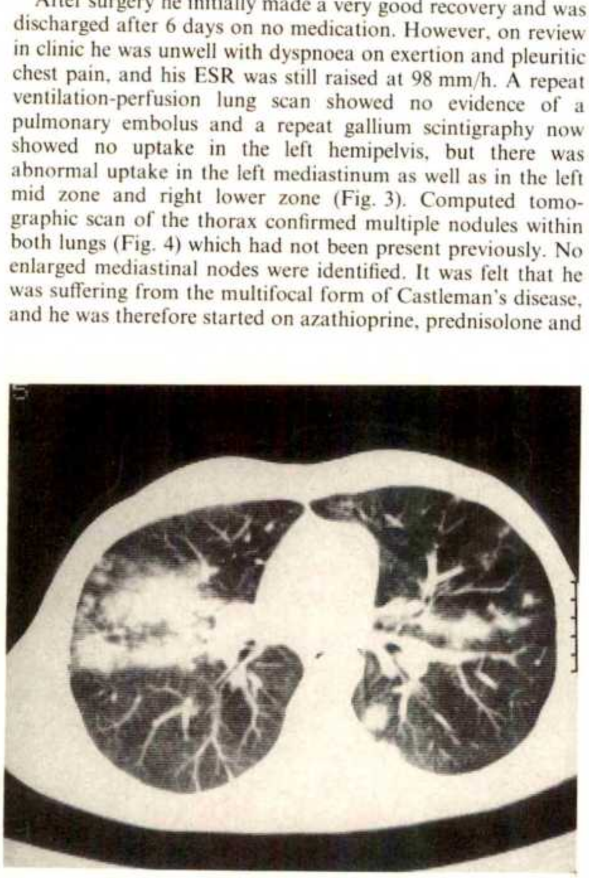

Figure 4. Thoracic CT scan showing multiple nodules within both lungs.

Discussion

Giant lymph node hypertrophy, also known as Castleman's disease, was first described by Castleman and Towne (1954). This case was of a localized tumour in the mediastinum with characteristic histology showing hyperplasia of lymphoid follicles and capillary proliferation with endothelial hyperplasia. Two histological types are now recognized: the hyaline vascular type (90%), as in Castleman's original case, and the plasma cell variant (10%), which is characterized by an abundance of plasma cells. The majority of cases (75%) occur in the mediastinum, but many other sites have also been reported. One that seems to have given great diagnostic problems has been Castleman's disease occurring in the retroperitoneum, where it may be difficult to distinguish from other benign and malignant tumours (Bartkowski & Ferrigni, 1988). The plasma cell variant is frequently associated with systemic side effects and in addition it is now recognized that there can be a multifocal form of the disease which tends to have a more aggressive course, sometimes requiring immunosuppressive agents to control it (Weisenburger et al, 1985). It is from this form of the disease that our patient was suffering.

The aetiology of this condition remains unknown (Frizzera, 1985). Analysis of the tissue shows no evidence of monoclonality, but in a number of cases the condition seems to progress to malignancy (Hanson et al, 1988). In addition, similar histology may be found in other conditions including AIDS and several autoimmune conditions. Its importance lies in the fact that it is benign and its localized form may be cured by surgery.

Initial diagnosis is often very difficult, especially as the patient may have no localizing symptoms attributable to the mass. Investigations are directed at localization but the diagnosis is usually only made with the help of histology. Plain radiography may reveal a characteristic pattern of arborizing calcification (Goodman et al, 1983), but CT and ultrasound are more useful investigations which may also show other sites of involvement in the multifocal form of the disease (Libson et al, 1988).

There has been no previous report of the use of gallium scintigraphy in the multifocal form of this condition. Wahner et al (1978) reported a case of localized Castleman's disease of the small bowel mesentery, initially thought to be an abdominal abscess, which was strongly positive on gallium scan. Histology of that case showed predominantly the hyaline vascular variant. Gallium scintigraphy is frequently used to investigate patients with intra-abdominal masses thought to be inflammatory in nature and Castleman's disease should be considered as a rare cause in the differential diagnosis. Once the diagnosis has been made, however, gallium scintigraphy may be useful in showing or excluding the presence of multifocal disease. In addition, in the multifocal form, as described here, as well as helping to make the initial diagnosis and define the sites of involvement, gallium scintigraphy may be of use in following both the course of the disease and its response to therapy.

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Neuroblastoma of the tail of the pancreas in childhood

J. C. Hoeffel, MD, M. A. Galloy, MD, *C. Schmitt, MD and †M. Schmitt, MD

Departments of Radiology, *Medicine II and †Surgery, Children's Hospital, Allée du Morvan, 54511 Vandoeuvre Cédex, France

Keywords: Pancreatic tumours, Children, Computed tomography, Ultrasound

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We report a rare case of this condition in a child 4 years old, with the computed tomography and ultrasound findings.

Case report

A 4-year-old boy presented with a firm, non-tender left upper quadrant abdominal mass. There was mild fever and moderate anaemia. Plain radiographs of the abdomen revealed an opacity in the left upper quadrant with calcification.

Abdominal ultrasound (Fig. 1) revealed the mass to be mainly densely echogenic and arising from the retroperitoneum. The left kidney and the left adrenal gland were separate from the mass.

Computed tomography showed a large heterogeneous mass (Fig. 2(a)) in the retroperitoneum with multiple calcifications. The anterior and medial contours of the tumour were indistinct. The posterior wall of the stomach seemed infiltrated and the pancreas could not be clearly defined (Fig. 2(b)). The posterior contours were well defined and distinct from the kidney.

Because of the calcification, the diagnosis of neuroblastoma was considered but the origin of the tumour could not be clearly established although it seemed to be the pancreas. Urinary catecholamine levels were normal.

At laparatomy, the tumour was posterior to the stomach, and was removed with the tail of the pancreas. The mesocolon was resected because it was intimately attached to the tumour.

Histological examination revealed that it was a Stage III neuroblastoma of 840 g, with a large necrotic area, invading the pancreas, without evidence of lymph node involvement but with local extension.

Although satisfactory removal of the tumour was achieved, because of the possibility of microscopic residue, radiotherapy was given (30 Gy) with chemotherapy for 1 year.

The child is well and free of disease 7 years later.

Discussion

Malignant tumours of the pancreas are rare in childhood. Tsukimoto et al (1973) reported 12 cases of

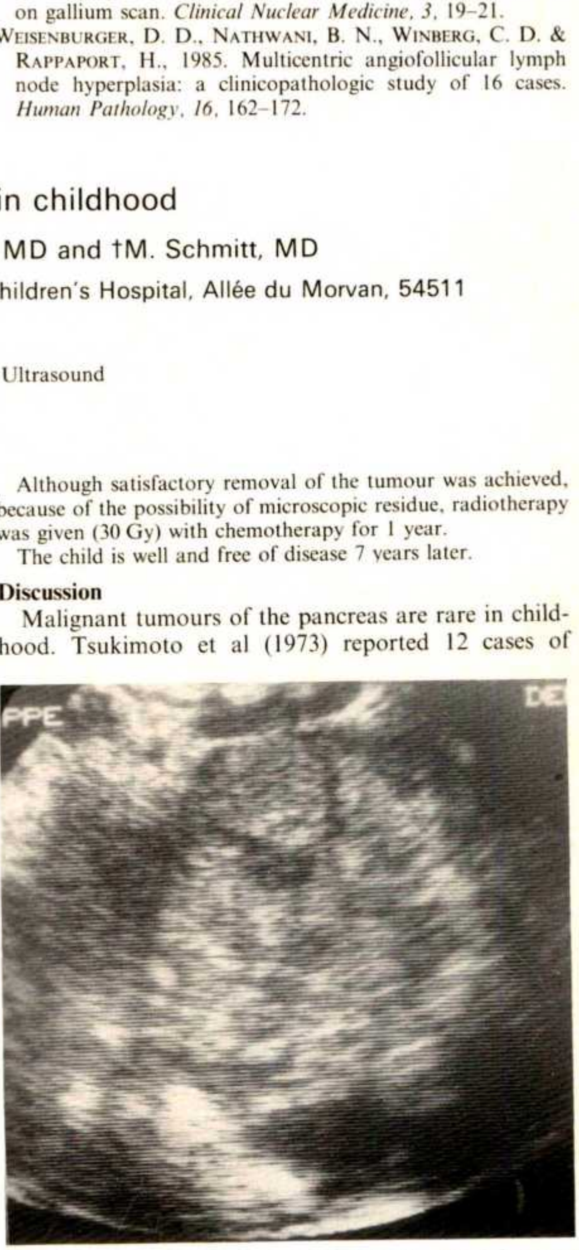
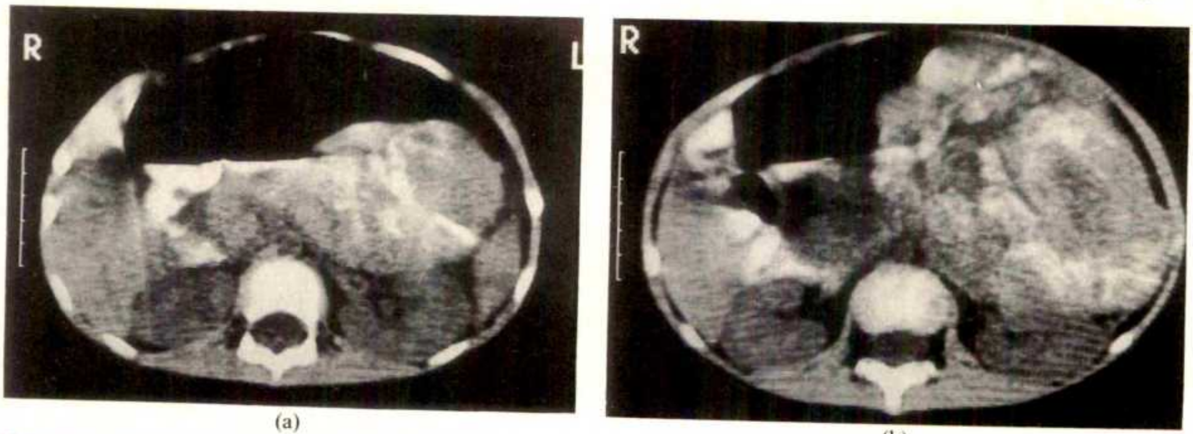


Figure 1. Well defined echogenic mass in the left upper quadrant.

Address reprint requests to J. C. Hoeffel, MD.



(a) (b)

Figure 2. (a) Heterogeneous mass with calcification. The posterior edge of the tumour is distinct from left kidney. (b) The anterior and medial borders of the mass are less clearly defined than the posterior edge, consistent with a pancreatic origin.

pancreatic carcinoma. Bienayme and Grosse (1975) reviewed from the literature 28 cases of malignant tumour, most carcinomas. Camprodon and Quintanilla (1984) were able to collect 28 cases of carcinoma of the pancreas from the Western literature while Lack et al (1983) reported five new cases of tumour of the exocrine pancreas in children and adolescents.

Of the 58 cases recorded by Rich et al (1986), approximately 70% were adenocarcinoma mostly located in the head of the pancreas, 20% were islet cell carcinoma and 10% were other malignant tumours arising in the pancreas. The most common clinical feature is a palpable abdominal mass.

Four cases of neuroblastoma have been reported:

a case of neuroblastoma in the head of the pancreas in an infant who died (Peychlova, 1973);

a case of ganglioneuroblastoma of the head of the pancreas in a girl 11 years old alive 3 years later (Romualdi, 1969);

a case of neuroblastoma of the head of the pancreas in a child 2 years old, alive 8 years later (Bienayme & Grosse, 1975);

a case of neuroblastoma of the head of the pancreas with lymph node involvement in a child 2 years old, alive 2 years later (Galifer et al, 1983).

Increased excretion of urinary catecholamines is present in many cases, and surgery with radiotherapy and chemotherapy is the treatment of choice.

Acknowledgment

The authors would like to thank Dr P. B. Guyer, Royal South Hants Hospital, Southampton, for his help.

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Case reports

Superior mesenteric artery branch aneurysm diagnosed by ultrasound

By Bhim Singh Verma, MD, Ajit Kumar Bose, MD, DMRD, DRM, Harish Chandra Bhatia, MD and *Ravindra Katoch, MS

Departments of Radiology and Surgery, Army Hospital, Delhi Cantt 110010, India

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Keywords: Ultrasound, Aneurysm, Superior mesenteric artery

Superior mesenteric artery (SMA) branch aneurysms are extremely rare (Jorgensen, 1985). Only 40 cases have been reported in the literature up to 1980 (Mourad et al, 1987). Most are diagnosed after rupture into the mesentery, the intestinal lumen or the peritoneal cavity (Reuter et al, 1968; Jorgensen, 1985). Occasionally they are found by arteriographic studies.

Only one case diagnosed by ultrasound has been reported in the literature (Grech et al, 1989).

We report a case of an aneurysm of a right sided branch of SMA diagnosed by ultrasound. Angiography confirmed this to be a middle colic artery aneurysm. Tuberculosis of lymph nodes was an associated finding.

Case report

A 19-year-old married woman presented with an abdominal pain that had started 6 months before. She also gave a history of fever in the evenings and gradual loss of appetite. She had lost 10 kg in weight during the course of her illness.

The patient was thinly built (height 150 cm, body weight 36 kg), pale and normotensive with a pulse rate of 102/min. She had significant lymph node enlargement in right cervical, both axillary and both inguinal regions. The abdomen was soft and a mass 6 × 5 cm was palpable just above the umbilicus. It was mobile, and transmitted pulsation from the abdominal aorta was evident. The liver and spleen were not enlarged, and no other mass was palpable in the abdomen. There was no audible bruit over the mass. All the peripheral arterial pulses were normal.

On admission her haemoglobin was 8 g/dl. Total leucocyte count was 9.2×10^9/l and the differential count showed 72% lymphocyte predominance. A chest radiograph was within normal limits. A lymph node biopsy from the right cervical area was taken.

Ultrasound examination of the abdomen revealed the presence of a mass 53 × 45 × 43 mm just above the umbilicus. It returned medium level echoes peripherally surrounding an oval anechoic area measuring 35 × 21 × 18 mm.

Very feeble expansile pulsations of the mass were observed on real time examination. On the left side the anechoic part of the mass tapered into a narrow channel to join the lumen of the SMA (Fig. 1). The abdominal aorta was normal; no para-aortic or mesenteric lymph node enlargement was detected. An echocardiogram revealed normal valves with no evidence of vegetation.

A diagnosis of right sided SMA branch aneurysm with peripheral thrombosis was made, and contrast enhanced CT scan confirmed the presence of the aneurysm but did not clearly demonstrate the communication with SMA.

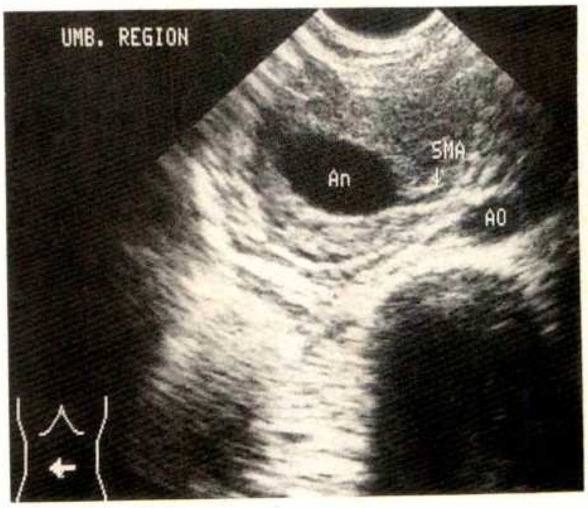

Figure 1. Transverse scan of the umbilical area of the abdomen showing a large aneurysm of a right sided branch of the superior mesenteric artery. An: aneurysm; AO: aorta; SMA: superior mesenteric artery.

The report of the right cervical lymph node biopsy revealed evidence of tuberculous involvement including the presence of acid fast bacilli. Routine blood cultures did not grow any organisms up to 72 hours.

In view of the bilateral inguinal and axillary lymph node enlargement, it was decided to defer angiography. Antituberculous treatment (ATT) was instituted and the aneurysm was closely observed on repeated ultrasound examinations. The patient showed good response to ATT, and the lymphadenopathy regressed sufficiently to permit an angiographic study after 4 weeks of treatment.

Angiography showed a normal abdominal aorta, coeliac axis and its branches, renal arteries and a slightly enlarged inferior mesenteric artery. A very large collateral (arcade of Riolin) was seen arising from the left colic artery, supplying the territories of middle and right colic arteries. The SMA showed a patent lumen up to 5 cm from its origin. A 3.5 cm segment of this artery was not visualized and the distal part of the SMA was supplied by a collateral from a jejunal branch. A large aneurysm measuring 35 × 24 mm was demonstrated in the region of the proximal part of the middle colic artery (Fig. 2).

At laparotomy the middle colic artery aneurysm was confirmed. It was treated by simple ligation on both sides of the

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*Present address: Unit of Vascular Surgery, Bristol Royal Infirmary, Bristol BS2 8HW, UK.

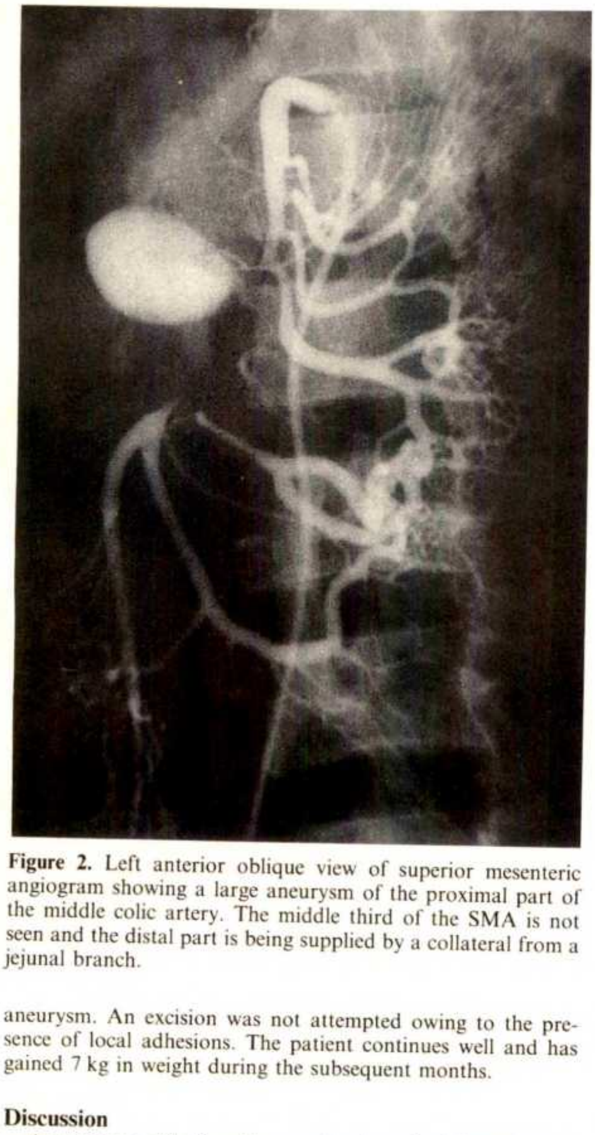

Figure 2. Left anterior oblique view of superior mesenteric angiogram showing a large aneurysm of the proximal part of the middle colic artery. The middle third of the SMA is not seen and the distal part is being supplied by a collateral from a jejunal branch.

aneurysm. An excision was not attempted owing to the presence of local adhesions. The patient continues well and has gained 7 kg in weight during the subsequent months.

Discussion

Aneurysms affecting the smaller intestinal branches of the SMA are responsible for 3% of all splanchnic artery aneurysms (McNamara & Griska, 1980). Reuter et al in 1968 were the first to draw attention to branch artery aneurysms. They found four such aneurysms in the course of 325 superior and inferior mesenteric angiograms. Aneurysms have been reported in all the branches of SMA: inferior pancreaticoduodenal, jejunal, ileal and colic (McNamara & Bakshi, 1982). Most branch aneurysms are small, measuring several millimetres to 1.5 cm in size. Aneurysms of jejunal, ileal and colic branches are intra-mesenteric or submucosal in location. Jejunal branch aneurysms are most common and 90% of these aneurysms are solitary, except for those unusually small lesions associated with connective tissue disorders (Stanley et al, 1986).

Four major aetiologies of SMA branch aneurysms are identified: atherosclerosis, arterial dysplasia, arteritis and infection (McNamara & Bakshi, 1982). Submucosal lesions are congenital in origin. Mycotic aneurysms account for 60% of aneurysms of SMA and the patients are generally young. The pathogenesis of mycotic aneurysms involves destruction of the arterial wall by infection. This infection is initiated by septic emboli from left sided bacterial endocarditis, implantation of bacteria in the media or vasa vasorum during bacteraemia, or by direct extension from adjacent infected sites. In the present case the aetiology is not clear, but mycotic aneurysm resulting from involvement of the artery by adjacent tuberculous lymph node infection is most likely. Abdominal pain, a common symptom, results from a mass effect on adjacent structures, expansion, rupture or bowel ischaemia caused by thrombotic occlusion or distal embolization. In most cases, the abdominal pain is not characteristic and may be mistaken for pancreatitis or cholecystitis. In contrast to non-specific abdominal pain, a triad of fever, abdominal pain and a pulsatile abdominal mass indicate a mycotic aneurysm (McNamara & Bakshi, 1982).

Physical examination is rarely diagnostic since most lesions are small and difficult to feel. In this patient a palpable mass was present and the examination was made easier by the emaciated state of the patient.

Only four cases of SMA aneurysms diagnosed by ultrasound have been reported (Luna et al, 1980; Bret et al 1985; Mourad et al, 1987). A branch aneurysm of SMA was diagnosed as a saccular aneurysm of SMA by ultrasound (Grech et al, 1989). Angiography revealed this to be an aneurysm of the inferior pancreaticoduodenal artery.

Arteriography is the definitive study for most mesenteric aneurysms. Delineation of collateral flow, location of the aneurysm and patency of other visceral arteries is important in planning therapy. Operative intervention is required because of the high incidence of rupture. Superior mesenteric artery branch aneurysms are treated by ligation or aneurysmectomy of extra intestinal lesions and bowel resection for intra-mural aneurysms (Stanley et al, 1986).

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Radiation induced extraskeletal osteosarcoma

J. P. Logue, MB, MRCP, FRCR and F. Cairnduff, MB, MRCP

Department of Radiotherapy and Oncology, Christie Hospital, Wilmslow Road Manchester M20 9BX, UK

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Keywords: Osteosarcoma, Radiation induced neoplasms

Radiation induced neoplasms are a well recognized complication of radiation therapy. Among these neoplasms osteosarcoma is not uncommon, classically affecting the skeleton. We report a case of extraskeletal osteosarcoma occurring in the nasal cavity following kilovoltage radiotherapy.

Case report

A 62-year-old woman presented with a 1 × 1 cm Basal cell carcinoma on the skin of her left upper nose. She was treated with a single exposure of radiotherapy to a skin dose of 20 Gy using 100 Kv (3 mm Al) at a focus–skin distance of 15 cm to a circular area of a diameter of 2 cm. She was reviewed 6 weeks later at which time the lesion had completely resolved.

She represented 14 years later with an 8-month history of painless swelling of her left upper nose, nasal obstruction and epiphora (Fig. 1). Examination revealed a hard fixed mass adjacent to the bridge of her nose. The overlying skin showed signs of radiation stigmata. Examination under anaesthetic demonstrated fullness of the upper part of the lateral nasal wall anterior to the middle turbinate. The clinical appearance was of a primary nasal cavity tumour. Biopsies were taken of this area. Histology of these revealed normal nasal mucosa with an infiltrate of malignant tumour composed of spindle, oval and polygonal cells forming abundant osteoid and woven bone consistent with osteosarcoma. It is our belief that the nature of the presentation and histology, together with the subsequent growth pattern, are consistent with this osteosarcoma being extraskeletal in origin (although ultimately the exact origin cannot be proven).

Three weeks later on admission for palliative radiotherapy the lesion had progressed rapidly with fleshy tumour exuding from the left nasal cavity and a proliferative ulcerated lesion arising from the upper nose and occluding the left eye (Fig. 2).

She was treated with palliative intent utilizing a single megavoltage anterior field encompassing all gross disease to a dose of 27.5 Gy in 4 fractions.

Following treatment there was an initial partial response but unfortunately this was not sustained and she died 6 months later with progressive local disease.

Discussion

Secondary neoplasms are an unfortunate but accepted complication of cancer therapy. Both haematogenous and solid tumours are recognized and of the latter sarcomas are well described. It has been reported that 5.5% of osteosarcomas presenting in one centre are the result of previous therapeutic or incidental irradiation (Huvos et al, 1984). The majority of

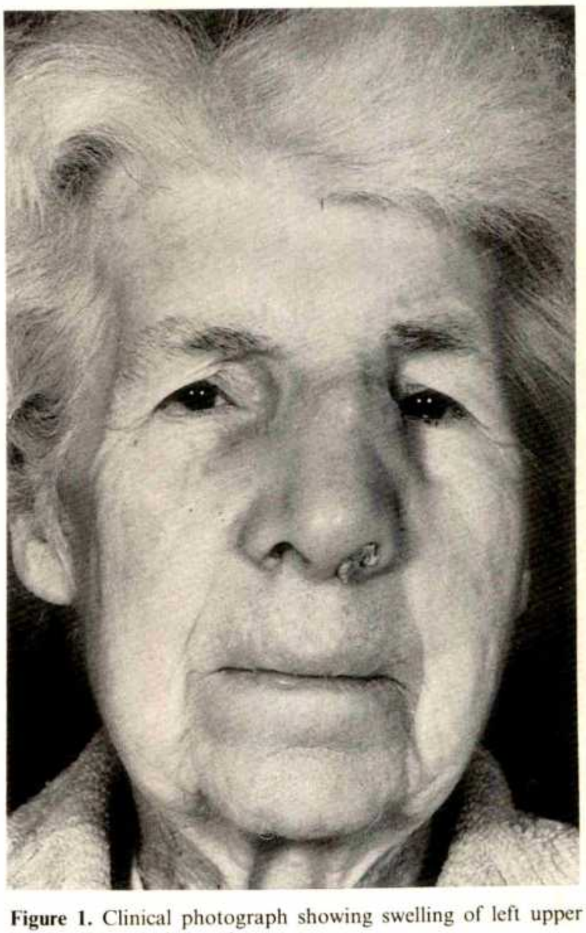

Figure 1. Clinical photograph showing swelling of left upper nose and nasal obstruction.

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*Author for correspondence.

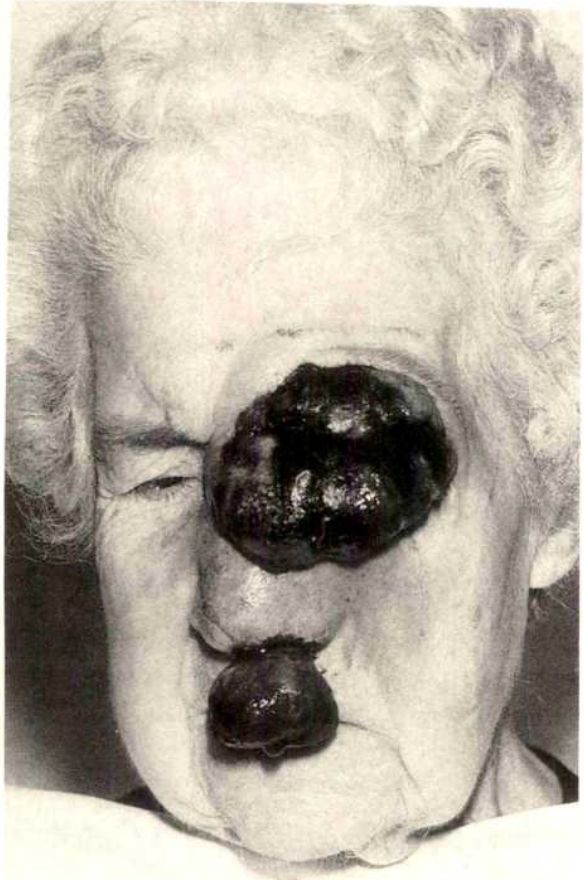

Figure 2. Clinical photograph showing tumour exuding from the left nasal cavity and lesion arising from the upper nose.

osteosarcomas arise within the skeleton with extraskeletal to skeletal ratio quoted as 1 : 25 (Allan & Soule, 1971).

Radiation induced extraskeletal osteosarcomas are rare with only 17 cases reported in the world literature by 1988. The majority of these cases occurred on the trunk with only two previous cases in the head and neck; one of which also arose in the nasal cavity. Only two previous cases have been reported following therapeutic radiation directed at skin conditions (Huvos et al, 1984).

The criteria for accepting the diagnosis of radiation induced osteosarcoma have been outlined by Cahan et al (1948) and are (1) the sarcoma must have arisen in an irradiated area; (2) irradiation must be followed by a relatively long latent period; and (3) there must be histological documentation. All these criteria are fulfilled by our patient. Boyer and Navin (1965) additionally suggested that there should be chronic radiodermatitis overlying the sarcoma. This latter criteria is also fullfilled but we would refute this as a requirement of diagnosis, particularly when skin sparing is now often sought in radiotherapy planning.

The mean latent period from exposure to development of sarcoma is approximately 12 years with cases arising from 6 to 24 years (Huvos et al, 1984). The reported case arose 14 years following treatment.

In the present case the tumour followed a virulent course with progressive local disease. Of the previously reported cases 9 out of 17 died of progressive local and or metastatic disease. The others are reported to be alive and diseases free from 1 month to 19 years following treatment.

Treatment of post-radiation osteosarcomas should be selected according to individual cases, but primary surgery is the treatment of choice in resectable lesions.

The reported case represents a serious late sequelae of radiotherapy. Quantification of the risk is necessary but unfortunately is unsatisfactory. Hadfield and Schultz (1970) estimated the risk of developing radiation induced bone sarcoma following radiotherapy for carcinoma of the breast to be about 0.2% of patients surviving for 10 years after therapy. There are however many possible sources of error leading to under-reporting of cases. The possibility of spontaneous sarcoma must also be remembered.

Only three cases of extraskeletal osteosarcoma, including this one, have arisen subsequent to radiotherapy directed at primary skin lesions. In our clinical practice we treat up to 1000 patients with skin lesions by radiotherapy each year and would strongly argue that the efficacy and convenience of this treatment heavily counterbalances the risk of development of this reported and other complications.

Acknowledgments

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Case reports

Intermittent inferior vena caval obstruction: an unusual cause demonstrated by ultrasound

By David F. Walter, DMRD, DipNB and Lakshmi I. Ramaiya, DMRD

Department of Radiodiagnosis, Christian Medical College and Hospital, Vellore 632004, Tamil Nadu, India

(*Received October 1988*)

Keywords: Inferior vena cava, Obstruction, Ultrasound

The syndrome of inferior vena caval obstruction may result from a number of diverse causes (Missal et al, 1965; Siqueira-Filho et al, 1976), and the clinical presentation and course depend, with some exceptions, upon the aetiology and level of obstruction. Thrombosis within the inferior vena cava (IVC) is one of the more common causes and may be primary or secondary to abdominal infection, abdominal trauma or surgery, hypercoagulable states or extension from femoral or iliac thrombophlebitis.

Real time ultrasonography is a simple, rapid and non-invasive technique for demonstrating the cause and level of IVC obstruction (Missal et al, 1965), as well as the adequacy of collateral circulation and the presence of intercurrent disease (Makuuchi et al, 1984; Park et al, 1985). We present a case of intermittent IVC obstruction with an unusual clinical presentation and, to our knowledge, a unique aetiology.

Case report

The patient was a girl, 6 years and 5 months old, who was admitted for investigation of recurrent episodes of swelling of the face, legs and abdomen.

She was well until the age of 1 year, when she developed peri-orbital swelling and abdominal distension which lasted for 3 days and then regressed spontaneously. Subsequent episodes occurred at intervals of 1–2 months and regressed either spontaneously or following medication. At the age of 3 years she was diagnosed as having nephrotic syndrome and was treated with steroids, which she took only intermittently. At 5 years she developed pedal oedema. She also had intermittent episodes of passing bulky, foul-smelling stools two or three times a day, for several years prior to admission.

She was the fourth child of an Rh negative woman whose first pregnancy ended in a stillbirth and whose next two were early neonatal deaths. The patient herself was icteric on the third day after birth and had one exchange transfusion, which was performed at another hospital and the details of which are not available. Her developmental milestones during infancy were normal.

At admission, the child was pale, had peri-orbital oedema, bilateral pitting pedal oedema up to the knee and abdominal distension with visible veins on the abdominal wall draining rostrally. The liver was palpable 3 cm below the costal margin and the spleen was enlarged 2 cm in its long axis. Free fluid was present within the abdomen.

Haemoglobin was 9.4 g%. The total white blood cell count was 13 200/mm^3 with a mild shift to the left. The total serum protein was 2.4 g/dl and albumin was 1.2 g/dl. Blood urea was 24 mg/dl and serum creatinine 0.4 mg/dl. Serum cholesterol was 107 mg/dl. The 24 h urine protein was 54 mg/dl. Serum bilirubin was 0.4 mg/dl and alkaline phosphatase was 184 units.

The possibility of inferior vena cava (IVC) obstruction was considered and an ultrasound examination was performed, which showed an irregular, highly echogenic mass about 4 cm in diameter situated within the right atrium and extending up to the IVC orifice (Fig. 1). There was a dense posterior acoustic shadow and the mass was seen to extend up to the hepatic vein opening (Fig. 2). The hepatic venous anatomy was normal. No collateral channels were seen.

At surgery, a friable mass, 5 cm × 4 cm, was present within the right atrium, extending up to the tricuspid orifice and protruding into the IVC. The mass was nodular and contained gross areas of calcification. It was excised and on microscopic examination was found to consist of fenestrated fibrin with hyalinized connective tissue and extensive calcification, consistent with an organized, partially calcified thrombus. No tumour or myxoid elements were found.

Post-operatively, the child recovered well and at discharge, 14 days after surgery, her total protein had risen to 3.6 g/dl and there was marked clearing of periorbital and pedal oedema.

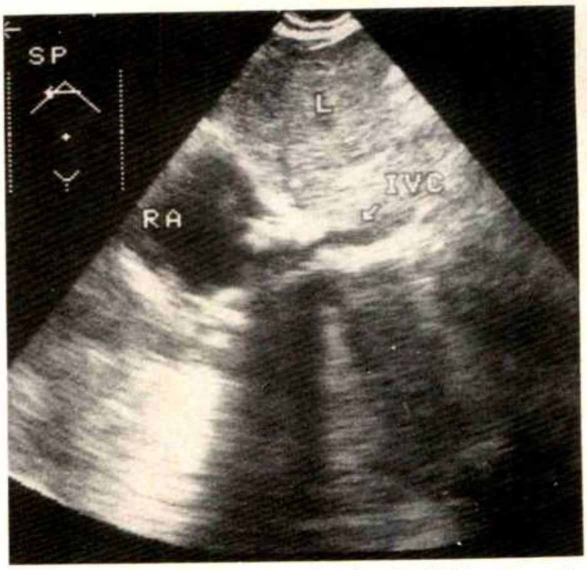

Figure 1. Midline sagittal scan showing the highly echogenic thrombus in the right atrium (RA) protruding into the IVC orifice.

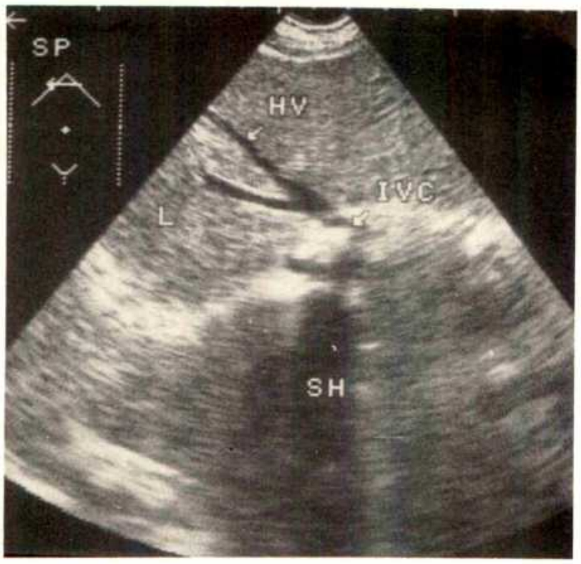

Figure 2. Dense acoustic shadowing (SH) from the thrombus resulting from the extensive calcification. The normal right and middle hepatic veins are seen.

Discussion

Exchange transfusion is performed by cannulation of the umbilical vein with a polyvinyl catheter to a distance of not more than 7 cm in a full-term neonate. When free flow of blood is obtained, the catheter is usually in a large hepatic vein or the IVC (Kernicterus, 1983).

The only well established late complication of umbilical vein catheterization is portal vein thrombosis, with subsequent development of portal vein obstruction and portal hypertension. This has been ascribed to the entry of the catheter into the portal vein rather than the IVC and to prolonged, traumatic or septic catheterization. Although it cannot be stated unequivocally that the portal hypertension is the result of portal vein thrombosis following umbilical vein catheterization, this conclusion seems reasonable when other causes of this condition are excluded. Similarly, in our patient, the absence of any other predisposing factors and the early onset of symptoms led us to the conclusion that the development of the right atrial thrombus represents a complication of the neonatal umbilical vein catheterization. Such a complication has not, to our knowledge, been previously described.

The typical sonographic features of right atrial thrombi are a non-homogeneous, immobile mass with a broad base of attachment to the atrial wall and a distinct intracavitatory origin (Manno et al, 1983). These criteria help to distinguish thrombus from myxomas, sarcomas, tricuspid valve vegetations and other right atrial lesions. Right atrial thrombus *per se* is uncommon and can occur in patients with dilated right atria, reduced cardiac output and in patients with stasis of blood, such as in congenital cardiomyopathy.

The other unique feature of the case is the production of intermittent IVC obstruction by protrusion of the thrombus into the IVC lumen. The ultrasound demonstrated unequivocally the cause of IVC obstruction and its level. The absence of any alteration in liver function may be attributed to the patency of the hepatic veins and their openings into the IVC, which also accounts for the absence of any intrahepatic venous collaterals, as described by Takayasu et al (1985).

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Case of the month

An unusual case of pneumonia

By R. Chaudhuri, FRCR

Queen Mary's Hospital, Roehampton, London SW15

(*Received September 1988*)

Keywords: Chest radiography

A 41-year-old European man presented with a 4-week history of increasing dyspnoea, left pleuritic chest pain, productive cough and 7 kg weight loss. He had smoked 60–70 cigarettes per day for many years, and he drank 3 pints of beer daily. He had had a myocardial infarction 5 years before, and had paranoid schizophrenia, well controlled on monthly flupenthixol injections.

On examination, he was pyrexial with signs of consolidation at the left lung base. There was no adenopathy. His fingers were heavily nicotine stained and his dental hygiene very poor. Investigations revealed a mild anaemia, elevated white blood cell count and ESR 100 mm/h.

An initial chest radiograph showed a left basal effusion loculated posteriorly (Fig. 1). What is the differential diagnosis at this stage?

He was discharged on trimethoprim, with some weight gain, erythrocyte sedimentation rate (ESR) 32 mm/h, but little resolution on chest radiography. Two months later he had developed a woody indurated mass over the left anterior ribs, with a central discharging sinus. He had again lost 3 kg, and the ESR had risen. Sputums were negative for acid-fast bacilli and malignant cells. Bronchoscopy was normal and bronchial biopsy and washings were unhelpful. No pleural fluid could be aspirated.

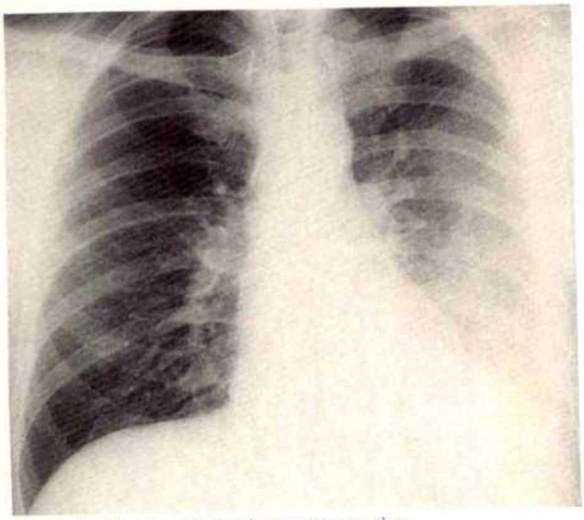
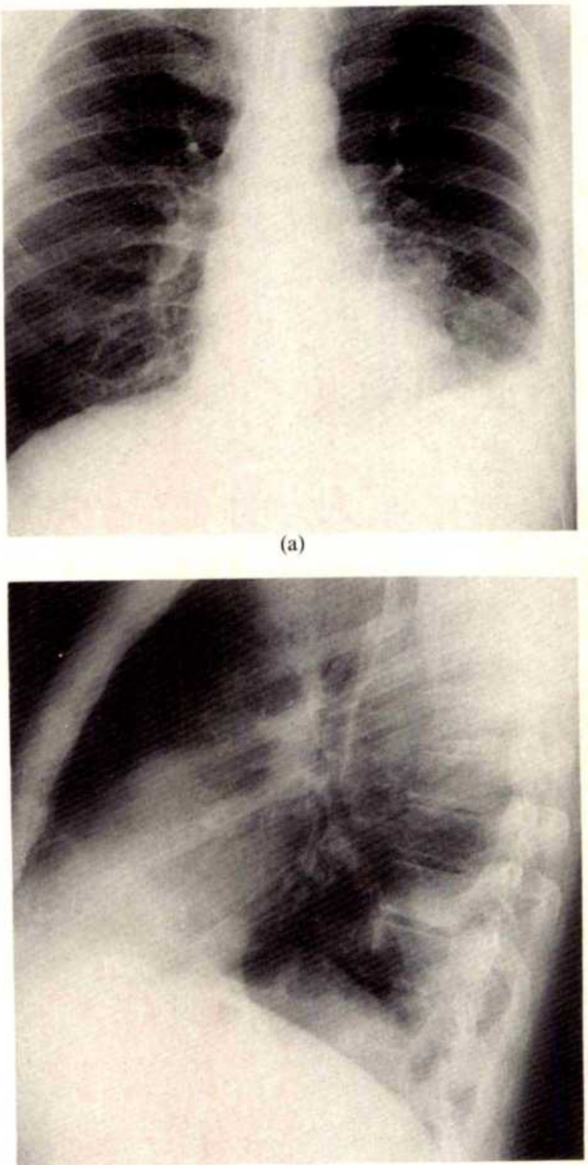


Figure 1. Chest radiograph on presentation.

The chest radiograph at this stage is shown (Fig. 2). How would you modify the differential diagnosis and how could the diagnosis be confirmed?



(a)

(b)

Figure 2. Chest radiographs after antibiotic treatment.

Current address: Department of Radiology, Guy's Hospital, London SE1 9RT.

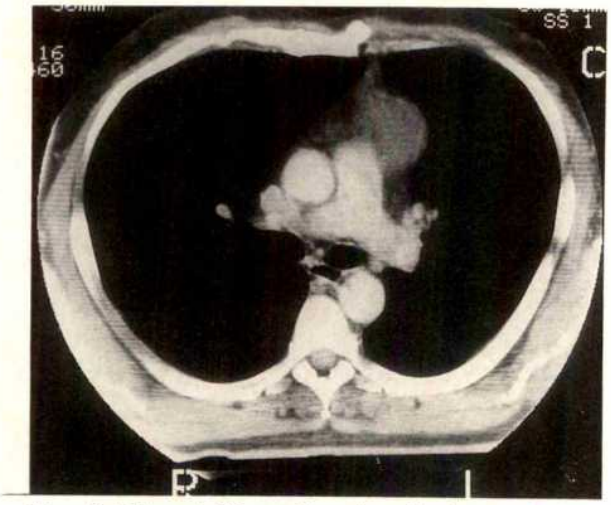


Figure 3. Enhanced CT scan through mediastinum at the level of the main pulmonary artery, showing lower extent of mass.

At presentation the differential diagnosis was of infection, including atypical pneumonias and tuberculosis, carcinoma of the bronchus with metastatic effusion or possibly pulmonary infarction or a collagen disorder. The second chest radiograph shows considerable pleural thickening over the left lower lobe with a solid looking mass posteriorly, with no associated rib involvement. In view of his history, the differential diagnosis was modified to either a neoplastic cause (including bronchial carcinoma with cutaneous metastasis, lymphoma or malignant mesothelioma) or a chronic infective cause (including tuberculosis, actinomycosis and fungal disease).

A diagnosis was made by gram-staining of aspirated sinus fluid and biopsy of the chest wall lesion, which revealed a 5 cm subcutaneous abscess. Pathognomonic sulphur granules of *Actinomyces israeli* were identified.

The patient was treated with high-dose tetracycline, continuously. One year later, the chest radiograph was almost completely clear. Four years later, however, he developed an anterior mediastinal mass. Computed tomographic (CT) scan showed a thymic mass (Fig. 3), which was found to be a thymic cyst, containing foci of neoplastic tissue in the lining. The patient remains well 1 year after surgery.

Discussion

Since the advent of antibiotics, actinomycosis has become increasingly uncommon. *Actinomyces israeli* is a saprophytic anaerobe existing freely in the mouth and upper respiratory tract. The usual source for thoracic disease is from carious teeth, infected gums, periodontal membranes and tonsils. Diagnosis depends on finding the sulphur granule which is a mycelium surrounded by radiating club-shaped rods. It produces proteolytic enzymes allowing penetration across usual anatomical boundaries.

Thoracic actinomycosis constitutes 15% of all cases. It is a wasting disease. Progressive lung infiltration and pleural involvement with fistula formation are common. Radiographic features in the chest, documented by Flynn and Felson (1970), are of a mass lesion, chronic alveolar infiltrate, pulmonary fibrosis, cavitation, pleural effusion or empyema. Spread is directly through the chest wall with associated wavy periostitis or frank rib destruction, or extension of pulmonary lesions across interlobar fissures. Dermal lesions may be local or peripheral (Webb et al, 1978). Sinus tracts on the chest wall may fistulize into the lung, pleural cavity, trachea, oesophagus or abdomen. Mediastinal widening, spinal involvement, pulmonary osteoarthropathy and erosion into blood vessels with haematogenous dissemination have also been described. Rarely, congestive heart failure, constrictive pericarditis, endocarditis and peripheral effusions occur secondary to direct spread from the pleura.

The radiological features of pulmonary actinomycosis are largely non-specific. Bates and Cruickshank (1957) suggested that periostitis of several adjacent ribs in the absence of empyema was the only pathognomonic finding, a view supported by Flynn and Felson (1970). However, only one of a series of six described by Frank and Strickland (1974) showed this sign, while none of six in Slade's series (Slade et al, 1973) or our patient showed periostitis.

A misdiagnosis of carcinoma of the bronchus or tuberculosis, with subsequent lobectomy or pneumonectomy has been well documented (Bates & Cruickshank, 1957; Slade et al, 1973). These studies have shown both bronchial carcinoma and pulmonary tuberculosis can co-exist with actinomycosis. However, association with a thymoma has not been described.

In summary, inappropriate antibacterial therapy or surgery may be prevented if pulmonary actinomycosis is considered at an early stage in unusually presenting pneumonias. The most valuable, but not the most frequent, radiological clues are a wavy periosteal reaction of the ribs and extension of lesions across interlobar fissures. Potentially more serious superadded or causally related complications, such as TB or malignancy and perhaps also thymoma, should be remembered.

Acknowledgments

I would like to thank Dr P. Frank and Dr D. G. Leaver for their advice and permission to publish this case.

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Short communications

Pulmonary embolus as a complication of therapeutic peripheral arteriovenous malformation embolization

By *P. McCarthy, MRCP, FRCR, A. Kennedy, MRCP, FRCR, P. Dawson, MRCP, FRCR and D. Allison, MD, FRCR

Department of Diagnostic Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS, UK

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Keywords: Pulmonary embolus, Arteriovenous, Embolization

Therapeutic embolization is an established technique in interventional radiology. In our unit we have considerable experience in the use of this technique in the management of systemic arteriovenous malformations. During the embolization of systemic vascular lesions containing arteriovenous communications, there is a danger of embolic material being swept into the venous side of the circulation and causing pulmonary embolism. In a previous study of 137 patients treated in this way, overt pulmonary embolism was observed to occur in two patients (1.5%); we did not, however, determine the incidence of subclinical embolism in that series and are unaware of any other available data concerning this (Hemingway & Allison, 1988).

A small pilot study was undertaken to see whether the incidence of subclinical embolization in these circumstances was sufficiently high to merit more detailed investigation.

Patients and methods

Ten consecutive patients referred for the therapeutic embolization of a peripheral arteriovenous malformation were examined by ventilation/perfusion scanning 24 hours after the procedure. Informed consent to the scan was obtained from all patients.

It was not felt that an additional pre-embolization scan to establish the baseline appearance of the lungs could be justified in this preliminary study.

The 10 patients were all embolized with two or more of the following agents: sterile absorbable gelatin sponge (Sterispon), polyvinyl alcohol particles (Ivalon), hypertonic dextrose solution and steel coils. The exact combination of agents employed depended on the nature and size of the lesion being embolized.

Results

Eight of the scans were normal, two showed multiple areas of ventilation/perfusion mismatch (*i.e.* defects of perfusion in areas of the lung that were normally ventilated) (Fig. 1). None of the 10 patients exhibited any clinical signs or symptoms suggestive of pulmonary embolism following therapeutic embolization. Of the two patients with abnormal scans, neither had a history of pre-existing lung disease and neither smoked. One was a 23-year-old male, the other a 41-year-old female. It is of some interest that in both the individuals with abnormal scans the operator suspected at the time of the embolization that some embolic material had passed into the venous circulation.

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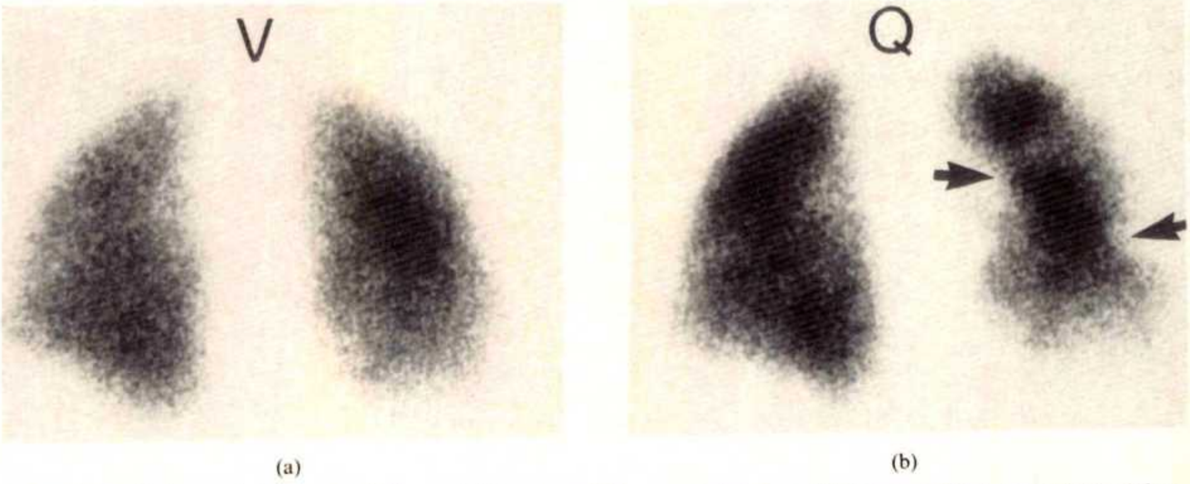
*Current address: Section of Uroradiology, Hospital of University of Pennsylvania, 3400 Spruce Street, Philadelphia PA19104, USA.



(a) (b)

Figure 1. Ventilation perfusion scan. (a) The ventilation scan (V) is normal; (b) the perfusion scan (Q) shows multiple defects (arrows) in the left lung.

A third patient in whom this occurrence had been suspected had a normal post-embolization scan.

Discussion

It seems reasonable to attribute the abnormal findings in these patients to embolization, though this can only remain a strong presumption in the absence of a pre-embolization scan. In order to establish the true incidence of subclinical pulmonary embolism following systemic embolization it would be necessary to undertake a controlled trial in which both pre- and post-embolization scans were performed in every patient.

It is difficult to justify such a study in patients with no clinical signs or symptoms referrable to pulmonary embolism and in whom any adverse long-term sequelae seem extremely unlikely, but the results of the pilot study reported here seem to suggest that subclinical pulmonary embolism probably does occur in a significant proportion of patients undergoing the therapeutic embolization of complex lesions containing arteriovenous shunts. The results, albeit in a small and uncontrolled series, underline the need for assiduous care and attention to technique during the embolization of arteriovenous communications and the need to terminate or modify the procedure if there is any suspicion on fluoroscopy that venous embolization may be occurring.

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Measurement of time-averaged flow in the middle cerebral artery by magnetic resonance imaging

By Maria Tarnawski, MSc, Soundrie Padayachee, PhD, Martin J. Graves, MSc, M. Graeme Taylor, PhD, Victoria T. Ayton, DCR(R) and *Michael A. Smith, PhD, FIPSM

Division of Radiological Sciences, UMDS, Guy's Hospital, London Bridge, London SE1 9RT, UK and *Department of Medical Physics, University of Leeds, Leeds General Infirmary, The Wellcome Wing, Great George Street, Leeds LS1 3EX, UK

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Keywords: Flow, MRI, Middle cerebral artery

Magnetic resonance imaging (MRI) sequences have been developed specifically for the quantitative evaluation of blood flow in vessels. The most promising sequences are those utilizing gradient field echoes to produce two interleaved images with a velocity-induced phase difference between images (Firmin et al, 1987; Ridgeway & Smith, 1987). Velocity values within a pixel can be extracted by subtraction of the images, producing a phase map where the phase is directly proportional to velocity. It is generally accepted that there is a lower limit to the size of vessel in which flow can be measured owing to the resolution restriction imposed by the image pixel size. This constraint is due to the partial volume effect, in which a pixel covering a vessel edge may contain both stationary tissue and flowing blood, and as a consequence produces limitations in the accurate measurement of vessel cross-sectional area.

Conventional methods of flow calculation generally combine a measure of the vessel cross-sectional area with the mean velocity. In small vessels, where the pixel size is a significant proportion of the vessel diameter, significant errors can occur in both the measurement of the mean velocity and, more importantly, in the cross-sectional area. In the latter a 10% error results in a 20% error in the flow.

The problems posed by the measurement of time-averaged flow using MR in small vessels can be solved using a simple theoretical evaluation of the partial volume effect. Under certain constraints the measured pixel phase is directly proportional to the velocity-induced phase and the proportion of the pixel occupied by the vessel. The measured phase, when combined with the pixel area, gives the flow in that part of the vessel. Summing the values in all pixels in a region of interest (ROI) containing the vessel then results in the flow rate. Thus area measurements are not required as long as we ensure that the ROI encompasses the complete vessel; in fact the ROI can be larger than the vessels. We have previously shown (Tarnawski et al, 1989), using *in vitro* phantom models where the pixel size to vessel diameter ratio simulates that of small vessels (0.1–0.4), that accurate flow measurements are possible using ROIs larger than the vessel and where a partial volume effect exists in a large proportion of the pixels. In addition the vessels need not be perpendicular to the slice.

This method has been used for the measurement of time-averaged blood flow in the middle cerebral arteries in normal asymptomatic volunteers. Measurement of flow in this vessel has not been possible previously using non-invasive techniques because of the inaccessibility and small size of these arteries. Other techniques such as transcranial Doppler ultrasound are used for measurements of the velocity (Kirkham et al, 1986) but flow cannot be measured as the temporal skull window, through which the beam passes, and the vessel orientation do not allow vessel visualization and therefore diameter measurements. Mathematical models have been used to suggest flow values in cerebral vessels (Zagzoule & Marc Vergnes, 1986) but are subject to simplifications and do not take into account the variable anatomy of the vessels.

Reprint address: Maria Tarnawski, Division of Radiological Sciences, UMDS, Guy's Hospital, London Bridge, London SE1 9RT.

Method

Measurements were performed using a 1.5 T imaging and spectroscopy MR system (Philips Gyroscan) using a flow-adjusted gradients (FLAG) pulse sequence (Groen et al, 1987). The phase image produced by the FLAG sequence results in stationary tissue with a zero phase, while blood flow has positive or negative phase depending on the direction of flow. An ungated continuous acquisition method was used (Tarnawski et al, 1990) which has advantages over the more usual gated methods in terms of reduced sampling interval, reduced acquisition and post-processing times.

In the measurement of time-averaged flow in small vessels the problem of partial volume can be overcome by choosing an appropriate velocity sensitivity for the FLAG sequence. A diagrammatic representation of the partial volume effect is shown in Fig. 1 where the proportion of the pixel occupied by the vessel is α. The phase due to blood flow, ϕ_v, is the average value of individual spin groups moving at different velocities within the vessel because of the velocity profile across the vessel. The pixel phase measured from the image, ϕ_m, is related to ϕ_v and α by the following equation:

$$\tan\phi_m = \frac{\alpha \sin\phi_v}{1+\alpha(\cos\phi_v - 1)} \qquad (1)$$

The velocity sensitivity should be chosen to produce a π phase change for a velocity which is at least twice the maximum expected velocity; this usually occurs along the vessel long axis. Pixels at the margins of the vessel have a small induced phase ϕ_v allowing simplification of the mathematical relationship above to the following (Tarnawski et al, 1989):

$$\phi_m = \alpha\phi_v \qquad (2)$$

If this criterion can be met then not only is the error due to the partial volume effect negligible for an individual marginal pixel but it can be extended to apply to the complete ROI. Thus pixels within an ROI larger than the vessel can be integrated to give the time-averaged flow, and an accurate measurement of the vessel cross-sectional area is not required.

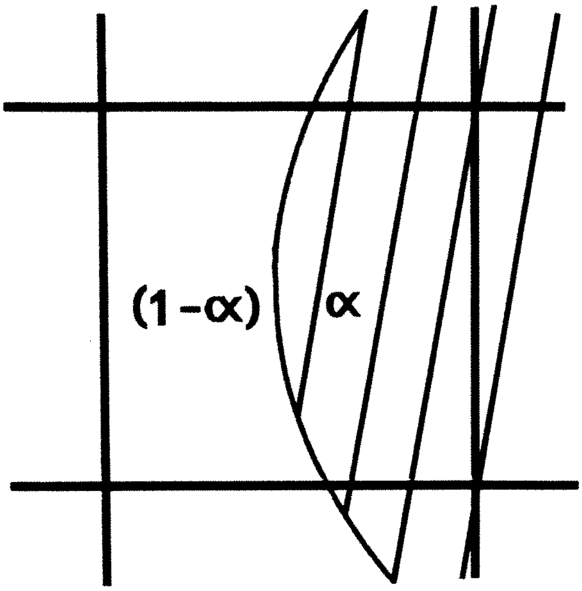


Figure 1. Diagram of a single pixel illustrating partial volume effect with a vessel (shaded) occupying a proportion α of the pixel volume.

Six healthy volunteers (four male, two female; mean age 28.3 years) were studied using a purpose-built radiofrequency coil consisting of two circular copper coils (10 cm diameter) placed on either side of the head. These were connected in parallel to a circuit enabling manual tuning and matching for each subject and provided a 70% improvement in signal to noise over the standard head coil for the region of the middle cerebral artery.

Several transverse spin–echo images were obtained to identify the cerebral arteries from which an oblique sagittal section, approximately perpendicular to the main stem of the middle cerebral artery, was used for the FLAG sequence. This sequence was modified to allow the gradient echo to be off-centred during the acquisition period resulting in reduced echo-times for thin slice, small field of view images, thus reducing intra-voxel phase dispersion.

The sequence parameters used were TR = 200 ms, TE = 19 ms, field of view 180–200 mm (depending on the subject head size), slice thickness 10 mm, flip angle of 45°, acquisition matrix of 256^2 pixels and four signal averages. In each subject a velocity sensitivity of 1.5 m/s was used to define the maximum velocity giving a π phase change. Both right and left arteries were studied and consecutive measurements of the arteries were made to assess the short-term reproducibility of the method; this resulted in a total investigation time of 30–45 min per subject. The complete procedure was repeated several months later for the long-term reproducibility.

Absolute flow rates were calculated from the phase images by identifying a square ROI which contained the middle cerebral artery. A similar ROI positioned over stationary tissue was used to calculate the background phase; the difference in the ROI values gave the phase which was subsequently converted to velocity. The flow rate was calculated from the sum of all pixel values in the ROI multiplied by the number of pixels and their area.

Results

Figure 2 shows a spin–echo transverse image of the middle cerebral arteries and the Circle of Willis with the position of the section for flow measurement superimposed. Figure 3 shows the velocity compensated field–echo image and the corresponding subtracted phase map showing the cross-section of the artery from which the flow measurements were made.

The MR flow values for the arteries are given in Table I. The mean error (coefficient of variation) of individual flow measurements, calculated from a combination of the inherent accuracy of velocity determination using the FLAG sequence

Table I. Time-averaged flow (ml/min) for the middle cerebral artery; the mean error is expressed as a percentage

Volunteer	Right		Left	
	Flow	Error	Flow	Error
1	84.6	3.7	114.3	4.0
2	73.0	5.1	42.5	5.6
3	162.3	4.2	85.4	4.5
4	83.7	3.7	163.0	3.2
5	117.9	3.6	127.2	3.3
6	191.9	3.2	123.9	3.3

Velocity sensitivity, 1.5 m/s.

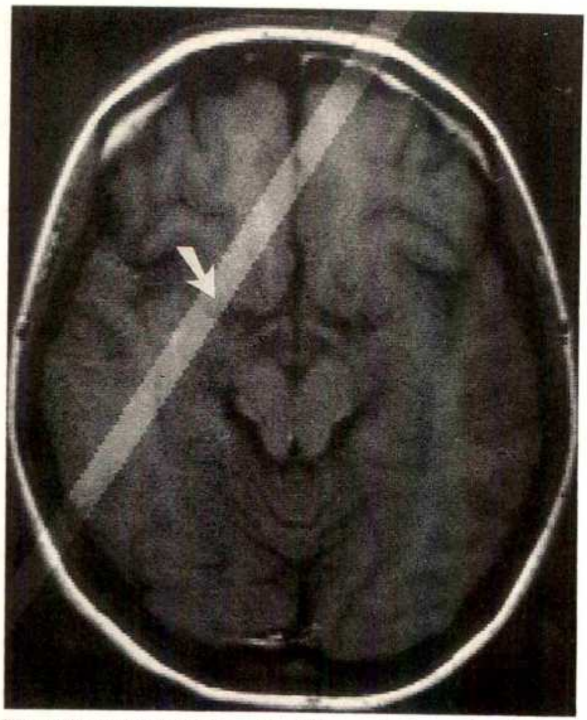


Figure 2. Spin–echo image of middle cerebral arteries showing the position of the oblique sagittal section chosen for flow measurements. The middle cerebral artery is indicated.

(Tarnawski et al, 1988) and the standard deviation of the background stationary tissue phase value ranged between 3.2% and 5.7%.

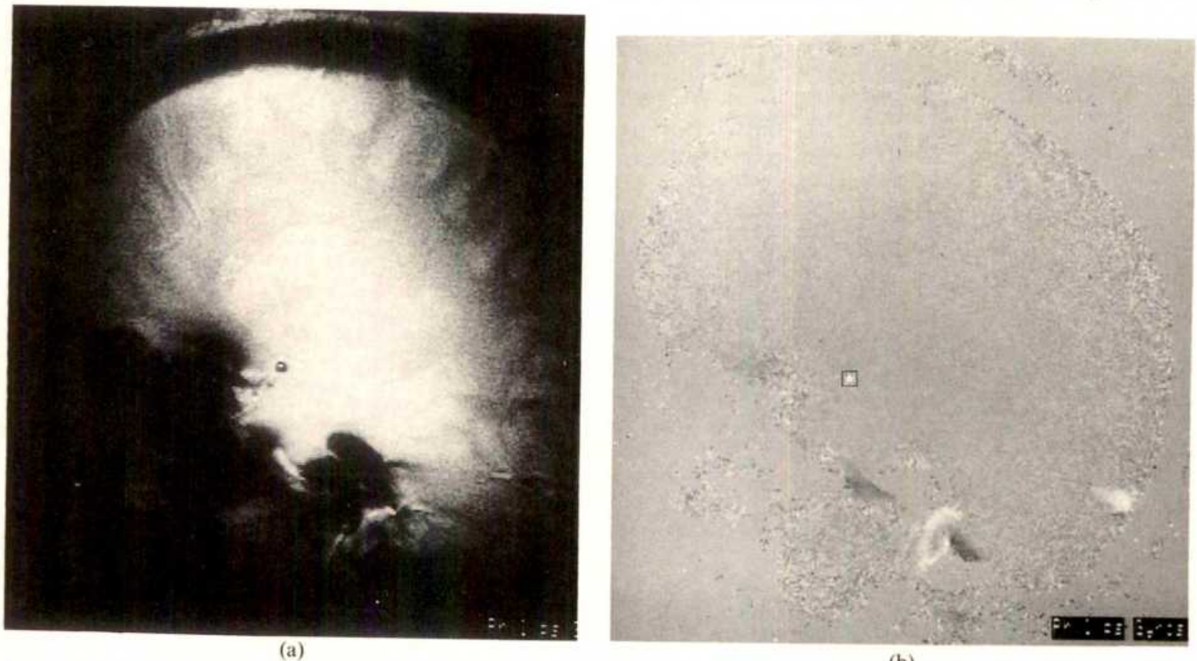
Repeated measurements on the normal subjects, both short term and long term, resulted in reproducibility values (coefficient of variation) of 9.9% and 9.3% respectively.

Discussion

Although there is no definitive technique for measuring blood flow in a specific cerebral artery to validate our technique, an approximation of middle cerebral artery flow may be derived from Doppler ultrasound and angiographic data. The time-averaged, mean velocity (intensity-weighted mean Doppler frequency) in the middle cerebral artery in the volunteers was 42±5 cm/s. The diameter of the middle cerebral artery in adults is known to be approximately 2–3 mm; therefore an indication of the range of values for middle cerebral artery flow would be 72–200 ml/min, and it is encouraging that the MR flow values are similar to this estimated value with the mean flow rate being 114 ml/min for both arteries.

The wide range of flow rates (42.5–191.9 ml/min) reflects to some extent the variability in mean velocity and vessel area between volunteers. The lower flow rates may be due to one of the problems of the ROI method in that a single pixel may possibly contain both artery and vein. Since the FLAG sequence assigns both positive and negative phases, the occurrence of artery and vein within a pixel will result in low or zero phase, thus underestimating the flow rate.

Another possible shortcoming of the method could be the reliance upon the fact that the velocity-induced phase is small, allowing the assumption of direct proportionality to be made. The choice of appropriate velocity sensitivity is difficult. Firstly the velocity sensitivity should be at least twice the maximum velocity that occurs at the edge of the vessel where the partial volume effect may occur. Secondly it should be greater than the peak systolic velocity in the vessel. The haemodynamics of



(a) (b)

Figure 3. (a) Field–echo image of the selected slice showing the middle cerebral artery. (b) Phase map of the selected slice; the ROI is shown positioned over the artery.

blood flow ensure that the velocity profile across the vessel is such that lower velocities are present near vessel walls, where partial volume effects will occur, resulting in small phases. Thus even if the maximum velocity in the centre of the vessel approaches the velocity sensitivity of the sequence, the constraints discussed earlier still apply in pixels at the edge of the vessel where the velocity is lower.

The typical pixel size in the phase images was 0.7 mm and, assuming a diameter of 3 mm, the pixel size to diameter ratio is 0.23; previous phantom experiments have shown that flow can be measured accurately with even higher ratios of 0.4. Thus the method may be applicable to smaller cerebral vessels if these could be located from the initial planning images.

The theoretical evaluation of the partial volume effect and its preliminary validation in normal subjects lead to the conclusion that, with the appropriate constraints on the flow sequence parameters, time-averaged flow can be measured in small vessels. Although caution may be necessary when using the ROI method in certain subjects with veins and arteries lying close together, it provides the first direct technique for measuring *in vivo* blood flow in the small cerebral vessels.

Acknowledgments

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Percutaneous femoral artery puncture: practice and anatomy

THE EDITOR—SIR,

I write to support very strongly the advice given by Drs Grier and Hartnell (1990) about the use of maximal femoral pulse for arterial puncture.

Although Dr Seldinger did not discuss this point in his original article (1953), the standard British accounts of Sutton (1962) and Saxton and Strickland (1964) make the point abundantly clear.

How did the false teaching begin?

Yours, etc.,
E. RHYS DAVIES

Department of Radiodiagnosis,
Bristol Royal Infirmary,
Bristol BS2 8HW

(Received August 1990)

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THE EDITOR — SIR,

The paper on percutaneous femoral artery puncture (Grier & Hartnell, 1990) discusses the various means used by angiographers to ensure a common femoral artery puncture. I was surprised to read that 39% of the angiographers questioned use the skin crease as a guide. Anyone doing femoral punctures regularly must soon discover how inaccurate this method is. The inguinal skin crease had been shown to bear no constant relationship to the inguinal ligament, the common femoral artery or the underlying bones (Lechner et al, 1988) Examination of old or obese patients shows how readily the skin moves in this area. I find it hard to believe that experienced angiographers anywhere today use such an inaccurate method to decide where to puncture, and I would like to ask Drs Grier and Hartnell exactly how they phrased their questionnaire, and in which order were the choices offered.

They conclude that the site of maximum pulsation is the most accurate localization of the common femoral artery. This may be true, but it is still not very accurate. They give a measurement of 6.5 cm for the distance between the inguinal ligament and the bifurcation of the common femoral artery. However, the position along the common femoral artery at which the wall puncture is made is crucial. The whole point of accurate puncture of the common femoral artery over the femoral head is to limit the possibility of pelvic or thigh haematoma, and to improve compression of the artery against the femoral head after the procedure. The angle of the needle path is particularly important in patients with a low inguinal ligament, increasing the risk of extraperitoneal bleeding. The diffuseness of the area of maximum pulsation in obese patients also reduces the accuracy of palpation. The skin entry site must always be lower than the desired artery wall puncture site.

I believe that in reality all angiographers use most of the visual and anatomical clues available to them, whatever they may say when questioned. I doubt if anyone ignores the maximum pulsation to puncture lower at the skin crease. Many angiographers will move the inguinal crease up over the site of maximum pulsation in obese patients to take advantage of thinner skin and subcutaneous tissues, but too great a distance between skin entry and arterial puncture site is not advisable.

I use palpation of the point of maximum pulsation and the position of the femoral head as landmarks. To identify the position of the femoral head, fluoroscopy is accurate and convenient. With a skin marker — a needle or scalpel blade — just below the site of the maximum pulsation to allow for needle angulation, a second of fluoroscopy confirms exact positioning. With the "last image hold" facility available on many current units, the added radiation dose is insignificant. An added benefit is confirmation that the unit is functioning before the puncture is made and technical difficulties encountered. Vascular calcification may also be identified.

I was taught to use this method routinely when training at the University Hospital in Zürich, and am sometimes impressed by the disparity between palpation and fluoroscopy. This usually leads to repalpation and a more considered puncture than either method alone.

Fluoroscopy to help decide the site of puncture is not described in the standard angiography texts, but is not new (Grossman, 1974). Other authors have also referred to its value for arterial (Srikantaswamy, 1984) and venous punctures (Baum et al, 1989) in the groin. A paper published recently (Spijkerboer et al, 1990) stresses the relationship of the common femoral artery to the femoral head, and while it followed that of Grier and Hartnell, the essential point made about the relationship of the femoral head to the vessels is not new. I find it strange that an anatomic study written by radiologists does not suggest the use of radiography to localize a vessel known to be closely related to a bony landmark.

I believe that fluoroscopic correlation of the position of the femoral head with the site of maximum pulsation is the best method to identify a safe common femoral artery puncture site.

Yours, etc.,
M. J. TOWERS

Department of Radiology,
Toronto General Hospital,
200 Elisabeth Street,
Toronto, Ontario,
Canada M5G 2C4

(Received October 1990)

Authors' reply

THE EDITOR—SIR,
We thank Dr Tower for his comments but is is no surprise to discover that 39% of the angiographers questioned used the skin crease as a guide. It is because so many people use the skin crease (remember that angiography is performed by cardiologists as well as properly trained radiologists) that this survey and the subsequent radiographic study was performed. The continued use of the skin crease persists in spite of the well documented inaccuracy of this as a reliable guide to femoral artery puncture. It should be noted that our report is the first to appear in the British literature and it is for this reason we carried out the study.

Our questionnaire asked which of the available landmarks (skin crease, maximum femoral pulse of bony landmarks) were preferred, either alone or in combination, to guide the level of arterial puncture. The letter covering this questionnaire commented on the variable position of the skin crease and the need to puncture the common femoral artery. If this was slightly to have biased the result in any way it would have been in favour of reporting the use of the pulse or bony landmarks rather than skin crease.

We disagree that the use of fluoroscopy is necessary in routine angiography. As far as the second author is concerned, in an experience of many thousands of retrograde femoral artery punctures the use of screening is hardly ever warranted. If this was to be used as a routine procedure it would simply slow down the case. We assume, and I think rightly, that our radiographers ensure that the X-ray fluoroscopy unit is functioning satisfactorily throughout the procedure. The detection of vascular calcification is of course irrelevant.

The only time when screening appears to be of any significant use is when performing antegrade punctures when a sufficiently high puncture site may be difficult to achieve, particularly with a fat patient.

It was our aim in performing this study to demonstrate the wide variations in practice which currently occur in the United Kingdom and the significant shortcomings of the use of the inguinal skin crease to guide femoral artery puncture. We believe that our study has confirmed that a large proportion of angiographers are using an illogical guide to their puncture site and should review their practice.

Yours, etc.,
D. GRIER
G. HARTNELL

Department of Radiodiagnosis,
Bristol Royal Infirmary,
Marlborough Street,
Bristol BS2 8HW
(Received October 1990)

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Ultrasonography in patients with suspected acute appendicitis

THE EDITOR—SIR,
It seems a pity that a paper with this title published in 1990 forgets the discussions of 2 years ago. Rosenquist (1988) showed that ultrasound reports with similar sensitivities, specificities and accuracies might in fact double the death rate from acute appendicitis if adopted. There was further commentary on this matter by Hillman (1988) and Drew (1988). Radiologists need a searching look at what they do for their patients — and for their papers.

Yours, etc.,
THOMAS SHERWOOD

Department of Radiology,
Addenbrooke's Hospital,
Hills Road,
Cambridge CB2 2QQ
(Received October 1990)

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Central venous catheter placement for intravenous digital subtraction angiography: an assessment of technical problems and success rate

THE EDITOR—SIR,
I read the article by Barber (1989) with great interest. I compliment the author for highlighting the frequently encountered but rarely reported problems related to central venous catheterization. Venous spasm in the arm is, indeed, a problem in catheterizing the cephalic vein, especially if J-guide wire is used. Some time ago, I switched over to using Radiofocus™ guide wire M (Terumo Corp., Tokyo) for catheterization of the right atrium by upper extremity venous route. In the last 100 consecutive unselected patients who underwent intravenous digital subtraction angiography (IV-DSA) by this route, I have used this guide wire and have seen no instance of

dissection and only two instances of venous spasm, both related to the cephalic venous puncture. The flexible tip of this straight-type guide wire is so soft that it entails virtually no risk of perforation or dissection and is extremely useful in crossing the shoulder girdle in cephalic venous punctures. In addition, the patients experience no pain, since this guide wire dose not seem to result in any intimal trauma. Contrary to the previous reports which mention that crossing the shoulder girdle after cephalic venous puncture is often difficult and time consuming (Dawson, 1988a, 1988b), I fully agree with Dr Barber that these difficulties can be easily overcome by changing the position of the arm, and that they should not bias a decision against a central venous injection site for IV-DSA.

Mediastinal or intercardiac extravasation has been previously reported with the use of straight and catheters and has been attributed to catheter recoil and jamming of the tip in a caval tributory (Rosen et al, 1983; Pinto et al, 1984; Arbona et al, 1985). Dr Barber mentions that pigtail catheters may minimize extravasation risks but catheterization success rate with pigtail catheters have not been reported. In this regard, I wish to state that we have been routinely using 5 F high-flow pigtail catheters for IV-DSA examinations (Cordis Corp., USA). During the last 410 consecutive IV-DSA studies, I have not encountered any instance of mediastinal extravasation. This is probably related to two factors: the use of pigtail catheters, and the use of the right atrium as the injection site. The advantages of using pigtail catheters are well known, and are related to its shape and the presence of multiple sideholes. It has been reported that pigtail catheters are both difficult and painful to insert and remove (Rosen et al, 1983; Pinto et al, 1984). However, I have never encountered any difficulty in either inserting or removing them, and the patients have never complained of any specific discomfort related to the procedure. The pigtail catheter must be removed after straightening the distal and by introducing a guide wire. Right atrium is a safe injection site for IV-DSA examinations (Sharma et al, 1988), provided that catheter position is checked in deep suspended inspiration prior to angiography. It should be placed in the mid-right atrium during deep inspiration. A catheter which lies in the upper or mid-part of the right atrium during test injection may shift to the superior vena cava in suspended deep inspiration during angiography and, thereby, risk mediastinal extravasation.

In conclusion, I agree with the author that upper extremity veins are a safe, convenient and time saving route for central venous catheter placement for IV-DSA examinations irrespective of the vein chosen for puncture. I wish to add that pigtail catheters are safe, easy to introduce and remove, result in no extra patient discomfort and overcome the potential hazard of mediastinal extravasation. Radiofocus™ guide wire M should be used for upper extremity venous catheterization since it overcomes the problems associated with venous spasm and dissection.

Yours, etc.,
S. Sharma

Department of Cardio-Vascular Radiology,
Catheterization Laboratory,
Cardiothoracic Centre,
All India Institute of Medical Sciences,
New Delhi, India

(Recieved September 1990)

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The variation of wedge factors with field size on a linear accelerator with wedge tray beneath secondary collimators

The Editor—Sir,

We refer to the recent technical note by Thomas (1990) in which the variation in wedge factor with field size was discussed. The linear accelerator used to produce the results in that article was a Dynaray LA 20 (Asea-Brown Boveri), in which the motorized wedge lies between the beam monitor and the movable, secondary collimators (Fig. 1a). We suggest that this wedge factor variation with field size may not occur with all designs of linear accelerator.

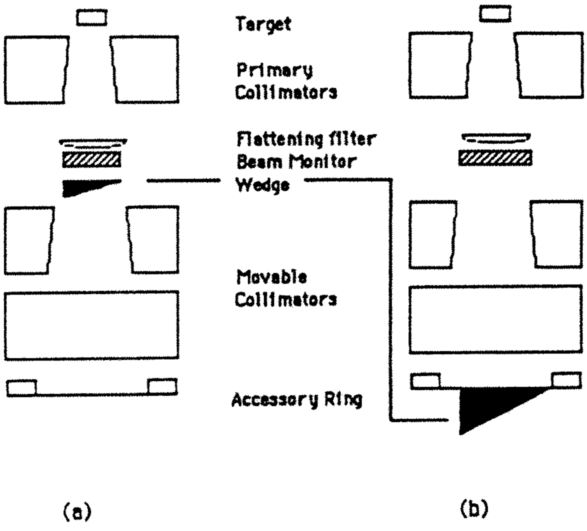

Figure 1. Position of wedge filter in the head of a linear accelerator: either (a) above or (b) below the movable collimators.

Table I. Wedge factors *versus* field size for a Varian Clinac 2100 C linear acclerator (maximum field size for a 60° wedge is 15 x 15 cm^2)

Photon energy	Wedge angle	Field size		
		3 x 3	10 x 10	15 x 15*/20 x 20
6 MV	15°	0.999	1.000	0.993
	30°	1.001	1.000	0.984
	45°	0.996	1.000	0.987
	60°	1.000	1.000	0.992*
18MV	15°	0.987	1.000	0.994
	30°	0.990	1.000	0.987
	45°	0.989	1.000	0.987
	60°	0.986	1.000	0.997*

Results from a Philips SL 75/14, with mechanical wedge above the secondary collimators, confirm up to 8% variation in wedge factor with field sizes between 3 x 3 cm and 20 x 20 cm.

We have investigated the variation of wedge factor with field size using a Varian Clinac 2100 c (Fig. 1b) and have not found as great a variation at photon energies of either 6 MV or 18 MV.

Measurements have been done for three square field sizes for each wedge angle: the minimum and maximum field sizes allowed for each wedge, and a 10 x 10 cm field as a reference size. Measurements were done in a water phantom at the depth of maximum dose for each energy, *i.e.* 1.5 cm and 3.0 cm for 6 MV and 18 MV photons, respectively. The source to surface distance was 100 cm, and the ionization chamber used was a 0.6 cm^3 Farmer chamber with 2571 dosemeter. The wedge factors quoted in Table I are the mean of measurements for both wedge directions and have been normalized to 1000 for a 10 x 10 cm field, for clarity. These results do not show the same trend to increase with field size and are always within 2% of the value quoted for a 10 x 10 cm field.

We believe this smaller field size dependence to be a result of the relatively large distance between the dose monitor chamber and the wedge so that much less scattered radiation from the wedge material reaches the chamber. The close proximity of the wedge to the dose monitor chamber in the Dynaray LA 20 and the Philips SL 74/14 would allow varying quantities of backscattered radiation to reach the dose monitor depending on the field size. We therefore conclude that no extensive wedge factor *versus* field size measurements need be done for the linear accelerators designed with a wedge mounted beneath the movable collimators.

Yours, etc.,

Elizabeth M. Dean
J. Bernard Davis

Departement fuer Radio-Okologie,
Universitaetsspital Zürich,
Raemistrasse 100,
8091 Zürich,
Switzerland,
(Recieved September 1990)

Reference

Thomas, S. J., 1990. The variation of wedge factors with field size on a linear accelerator. *British Journal of Radiology*, *63*, 355.

Dosimetry of electron backscatter at mandibular reconstruction in megavoltage photon beam

The Editor—Sir,

The dosimetry article by Delacroix et al (1990) in the August issue of *BJR* demonstrates the ignorance evident when proper literature search is not thoroughly conducted before starting a project. They reported a very superficial aspect of the dose perturbation caused by metallic mandibuilar reconstruction plates (MRP). Their data is redundant and incomplete.

A dose perturbation exists at and near interfaces between two dissimilar atomic number media exposed in a radiation beam. Hence any metallic object in an irradiation field will produce a dose perturbation. The metal–soft-tissue interface problem has been discussed by various research groups in the past. Some of the references can be seen in the articles by Das and Khan (1989) and Werner et al (1987). The dose perturbation is associated with the transport of the secondary electrons on both sides of the interfaces. Werner et al (1989) presented a general overview of forward and backscatter dose perturbations, whereas Das and Khan (1989) presented a detailed study of the backscatter dose perturbation. The backscatter dose perturbation significantly affects the dosimetry in the vicinity of the interface. In general, backscattter dose is a function of several variables:

$$\text{Backscatter dose} = f\,(E, A, w, d, t, x, Z, q) \qquad (1)$$

where f stands for the function, E is the photon beam energy, A is radiation field size, w is the width of the metallic inhomogeneity, d is the depth (position) of the interface, t is the thickness of the inhomogeneity, x is the distance away from the interface, Z is the atomic number of the inhomogeneity and q is the angle of the beam. Even though some of the parameters were discussed by Klevenhagen et al (1982) and Lambert et al (1982) for electron beams, the complete photon beam data were not available before the detailed presentation by Das and Khan (1989). Only a few of the parameters are reported by Delacroix et al (1990) in the context of MRP.

It should have been noted that TLD chips could not be used for the backscatter perturbation measurements unless used with ultra thin TLD chips or fine microscopic powder. The field size independence is indeed true for most energies and media which suggests that backscatter dose in a photon beam is purely due to secondary electron backscattering. An analysis of the different components contributing to backscatter perturbation was presented by Das and Khan (1989). Delaxroix et al (1990) speculated that the perforation in MRP might produce higher dose due to scattering. However, Das and Khan pointed out that, as long as the width, w, is greater than 3 mm, backscatter dose is independent of the width. The perforation of MRP in fact will have minimal perturbations and probably will have cold spots. Some of the factors studied by Delacroix et al are complimentary to the results presented by Das and Khan using similar methods.

Dependence of backscatter dose does seem to be contstant with respect to metal thickness, t. However, it is a steep function (see Fig. 6, Das & Khan, 1989). The saturation thickness is a linear function of the beam energy. It also depends on the beam energy but it is not a strong function. Delacroix et al noted that the backscatter dose is localized to 3–5 mm from various Z-valued materials. However, dose perturbation *versus* distance x away form interface is a complex function of atomic number Z and beam energy (see Fig. 7, Das & Khan, 1989). For high energy at a lead interface, backscatter dose can be seen up to 10–15 mm.

In the transmission side or forward direction, the dose perturbation is more complex. For low energy there is a cold spot but for at high energy there is a hot spot (Werner et al, 1987). The cut-off energy where this transition takes place is approximately 10 MV. Using analytical equations presented by Das and Khan, MRP dosimetry can easily be calculated for any material and hence further measurement is not warranted.

Yours, etc.,
INDRA J. DAS

Department of Radiation Oncology,
University of Massachusetts Medical Center,
Worcester,
MA 01655, USA
(Received September 1990)

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Related articles?

THE EDITOR—SIR,

Reading the paper of Tokita et al (1990) gave me a powerful sense of déjà vu. In concept, justification, basic experimental methods, central results and discussion of implications and applications, it bears an uncanny resemblance to another "Short communication" published in *BJR* in 1987. As a member of the Editorial Board, I hesitate to say it, but since the current authors do not even cite the earlier reference, it would appear both they and your referees are guilty of inadequate scrutiny of the literature! As *Private Eye* would no doubt put it, could these articles perhaps be related? I think we should be told.

Yours, etc.,
PETER DAWSON

Royal Postgraduate Medical School,
Hammersmith Hospital,
Du Cane Road,
London W12 ONN
(Received September 1990)

Author's reply

THE EDITOR—SIR,

We sincerely regret that we inadvertently missed a paper by Dawson et al (1987) on iodine photoactivation before we sent our paper to *BJR* for publication. Our experimental approach as well as conclusions are similar to those stated in that paper and we apologize for unintentionally omitting it as a reference in our paper.

Yours, etc.,
N. TOKITA

Department of Radiation Therapy,
National Cancer Center Hospital, 5-1-1,
Tsukiji, Chuo-ku,
Tokyo, Japan
(Received October 1990)

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William Hampson (1854–1926)

THE EDITOR—SIR,

Hampson was the originator of modern air-liquefaction methods, pioneered the prospect of heart pace-makers, made improvements in X-ray radiography and published, *inter alia*, a 70 000 word critique of the credit system, with his own proposals for reforming society.

An account of his achievements (Davies, 1989) lacks information on Hampson's family, personal relations and, especially, the scientific contacts that could have activated and guided this classics graduate who became a barrister.

Would any reader able to suggest sources of Hampson, or actually able to provide information on him, please communmnicatie with me?

Yours, etc.,
MANSEL DAVIES

14 Marine Terrace,
Cricceith LL52 OEF
(Received October 1990)

Reference

DAVIES, M., 1989. William Hampson. *History of Science, 22*, 63–73.

Proceedings of the British Institute of Radiology

Cracking gallbladder and bile duct problems

Abstracts presented at a meeting organized by the BIR Diagnostic Medthods Committee, held at the British Institute of Radiology, 36 Portland Place, London W1N 4AT on Thursday, 18 October 1990
This meeting was generously supported by Philips Medical Systems

Chairman: A. Adam
Oral dissolution therapy for gallstones, by J. R. F. Walters
A surgical perspective, by R. C. G. Russell. Abstract not received
Extracorporeal shock-wave lithotripsy, by P. R. Mueller, Abstract not recevied
Contact dissolution and percutaneous cholocysto-lithotomy, by W. R. Lees. Abstract not received

Chairman: R. Dick
New endoscopic approaches to bile duct stones, by D. Martin
Percutaneous and combined approaches to common bile duct and intrahepatic stones, by R. Dick
Surgery for bile duct cancer—palliation or cure? by I. S. Benjamin
Recent advances in percutaneous management of malignant obstructive jaundice, by A. Adam

Oral dissolution therapy for gallstones

Julian R. F. Walters
Royal Postgraduate Medical School

Gallstone dissolution with oral bile acid therapy is an attractive alternative to conventional surgical operations. Gallstones result from metabolic disturbance; reversing this metabolic problem seems a logical treatment. In patients with cholesterol gallstones, the bile is invariably supersaturated with cholesterol and oral bile acid therapy aims to reverse the process of cholesterol crystalization. Chenodeoxycholic acid (CDCA) and urodeoxycholic acid (UDCA) inhibit biliary cholesterol secretion and desaturate bile. Current therapy combines these in half the monotherapeutic dosages to preserve the dissolution efficacy of CDCA while minimizing side effects. Usual daily dosages are approximately 7 mg/kg of UDCA given together at bedtime. Selection of patients and stones is crucial for a successful outcome. A patent cystic duct is necessary and only cholesterol stones can be dissolved. Computed tomography (CT) scanning is the most sensitive method to screen out calcified mixed or pigment stones. Only small stones (less than 10–20 mm) can realistically be treated as dissolution is slow, taking up to 24 months. Consequently, only 20% of symptomatic patients have gallstones which are suitable for oral dissolution. To ensure complete dissolution, therapy needs to be continued for 6 weeks after the first clear ultrasound. Recurrence occurs in about 11% in the first year but is easily treated with further oral therapy. In the small proportion of patients with small, non-calcified cholesterol stones, oral bile acid therapy is a safe, non-invasive and effective outpatient treatment.

New endoscopic approaches to bile duct stones

D. F. Martin
Department of Radiology, University Hospital of South Manchester, Manchester M20 8LR

Endoscopic sphincterotomy (ES) is the primary method of managing common bile duct stones in patients who have previously undergone cholecystectomy and in elderly patients who are considered at high risk from surgery. Although 90% of patients have their bile ducts cleared following ES, not all are cleared immediately. Infective complications are directly related to failure of clearance of stones from the duct. Attempts at clearance should always be made and biliary drainage established if this fails. Other techniques are available to increase the chances of bile duct clearance and to avoid stone impaction. Mechanical lithotripsy allows clearance in 60% where stones are too large to pass through the sphincterotomy. The per-nasal catheter prevents stone impaction in the short term and can be sued to perfuse the duct with water, allowing small fragments to pass in over 80%. Duct perfusion is less successful with multiple and larger stones. Instillation of MTBE for contact dissolution through the per-nasal catheter is appropriate in a minority with cholesterol stones but can be effective. The per-nasal catheter allows cholangiography for visualization of stones during extra-corporeal shockwave lithotripsy which is successful in assisting duct clearance in 66%. When all fails, a biliary stent prevents stone impaction and can be used for long term management, although occasional (approximately 5%) patients suffer cholangitis. For the future, direct contact lithotripsy (electorhydrolic, laser) may improve common duct clearance further.

Percutaneous and combined approaches to common bile duct and intrahepatic stones

R. Dick
Royal Free Hospital, Pond Street, Hampstead, London NW3

The interventional radiologist has much to offer with such problems. Up to 5% of patients having a cholecystectomy present with residual stone(s) in the biliary ducts. Should an adequate T-tube access be possible, the radiologist can be expected to clear the stones using a steerable catheter, a basket, or a choledochoscope (FG 17) in 70–90% of patients. Should there be no T-tube access, and the endoscopic route is impossible or fails, then a transhepatic approach to duct calculi is feasible, whereby a combination of dissolution therapy, crushing with mechanical or contact lithotripsy, laser tripsy, pulsed saline irrigation and basket retrieval usually succeeds. Strictures below stones must first be dilated with 8 mm or 10 mm biliary balloon catheters (Meadox, Inc). Dilatation balloons or occlusal balloons themselves may be helpful in displacing the stones into the bowel, perhaps after a sphincterotomy performed from above using a balloon catheter or a papillotome. Patients with extensive lithiasis affecting all of the intrahepatic as well as the extrahepatic ducts are a special problem, as the disease recurs. Approaches include multiple percutaneous catheterizations into the segmental ducts of both right and left lobes, and repeated sessions to extract the numerous calculi. A combined approach may be preferred with either the creation of a subcutanedous stoma allowing access to a Roux-loop and thence retrograde approach to the bile ducts, is a recommended option. Percutaneous and trans-T-tube access are low risk procedures in experienced centres, with zero mortality. Cholangitis is invariable in many of these patients, and must be anticipated as well as dealt with promptly with appropriate, and sometimes rotating, antibiotics.

Surgery for bile duct cancer — palliation or cure?

I. S. Benjamin
Department of Surgery, King's College School of Medicine & Dentistry,King's College Hospital, London SE5 9RS

Hilar cholangiocarcinoma is a difficult clinical problem. Patients presenting with obstructive jaundice due to hilar strictures must be assessed carefuly to assess (1) whether the stricture is truly malignant (9% of patients presenting to our Unit were not), (2) whether the tumour is resectable and (3) the best method of palliation for unresectable tumours. Assessment must include definition of the extent of involvement of hepatic ducts involvement, involvement of portal vessels (and to a lesser extent hepatic arteries), direct spread to the liver and the atrophy/hyperplasia complex. All of the above may define resectability. Resection with curative intent was carried out in 40 out of 196 patients (20%) over a 10-year period, but only half of these had clear margins on final histology. Survival was significantly better for these patients than for those with involved margings (actuarial survival at 5 years almost 40%). When resection is impossible either surgical bypass (to the segment III duct) or percutaneous or endoscopic intubations is appropriate, with or without radiotherapy. Using these techniques we have achieved internal drainage in 78% of 51 patients from 1979–1983, and 88% of 77 patients from 1984–1989. A range of techniques should be available in centres treating this condition, and treatment tailored to the individueal patient. Multiple trials of radiotherapy in patients treated with or without resection are in progress.

Recent advances in percutaneous management of malignant obstructive jaundice

A. Adam
Royal Postgraduate Medical School, Hammersmith Hospital, London

External catheters for percutaneous biliary drainage are associated with several problems including pain and infection at the skin entry site and occasional leakage of bile. In addition they are a constant reminder to the patient that he has a terminal malignant condition. Biliary endoprostheses are completely internal and are not associated with most of the problems seen withexternal catheters. Conventional plastic stents are best inserted a few days after internal/external drainage has been established when a track has formed through the liver. This makes insertion much easier and probably reduces the incidence of complications such as haemobilia. The rate of occlusion of biliary endoprostheses is inversely related to the calibre of the stents. Most plastic stents in current use are 12 French gauge of 14 French gauge in size. Plastic endoprostheses usually become occluded approximately 5–6 months after their insertion. If they protrude into the duodenum they are best changed endoscopically. If the lower end of the stent is above the ampulla of Vater the endoprosthesi can still be changed relatively easily and a variety of percutaneous methods have been described. In recent years self-expandable metallic biliary endoprostheses have become available. These are delivered through small calibre sheaths or over small calibre catheters in a contracted state and when released across the obstructing lesion they expand to a large internal diameter. Thus they combine the advantage of a small track through the liver and a large lumen stent which is less likely to become occluded due to bile encrustation.

A report of this meeting is given in the BIR Bulletin at the back of this issue of *BJR* (p. B18)

1991, *The British Journal of Radiology*, *64*, 189–192

Book reviews

Techniques in Diagnostic Imaging (Second Edition). Ed. by G. H. Whitehouse and B. S. Worthington, pp. viii + 504, 1989 (Blackwell Scientific Publications, Oxford), £39.50.
ISBN 0-632-02453-4

This is the second edition of a now well established book. It comes 6 years or so after the first edition with a change of name, substituting "Imaging" for "Radiology". It has increased in size from 361 to 504 pages but does not, for all that, seem very much bulkier. Much of the original excellent content remains unchanged, but new sections are included on important topics such as digital subtraction angiography, ultrasound and computed tomography (CT). There is also a short chapter by Dr Oscar Craig on the medico-legal aspects of radiological procedures—unfortunately an important addition. New contributors include Dewbury, Golding, Craig, Hemingway, Freeman and Gregson.

This already excellent book has been even further improved and is to be recommended as, if not the cheapest, then certainly the best currently available book on radiological techniques. The editors in the preface to the first edition envisaged it being "a useful guide to all radiologists, especially those in training, and will provide an encapsulation of many facts which are otherwise disseminated throughout the radiological literature". This original intention has, I think, been fulfilled.

A few minor constructive criticisms might be made. There is very little on the technique of such interventional procedures as angioplasty, which are now no longer performed only in specialized centres by a few individuals but very widely. Perhaps in the inevitable third edition there should be interventional techniques.

I have one personal complaint. The excellent chapter by Nicola Russell on barium sulphate has been dropped from the second edition. It may be that this was a little too detailed for a book of this kind, but it did represent just about the only readily available source material on this subject. Some of the basic facts concerning barium suspensions are excellently covered by Clive Bartram in his section, but not nearly so much ground is covered. I, and I am sure others, always advised trainee radiologists who wanted to learn something about barium suspensions to refer to this book. Now we will have to suggest they get hold of the old edition!

P. DAWSON

Computed Tomography and Magnetic Resonance Tomography of Intracranial Tumours (Second Edition). Ed. by E. Kazner, S. Wende, T. Grumme, O. Stochdorph, R. Felix and C. Claussen, pp. xiv + 685, 1989 (Springer-Verlag, Berlin), DM660.
ISBN 0-387-50576-8

This is the second edition of a volume first published in 1982. It has been extensively revised and the dimension of magnetic resonance imaging (MRI) added. The textbook represents a distillation of experience gained in three German University Hospitals, based on a clinical population of 8516 gathered between 1975 and 1986. The book is actually concerned with mass lesions of all kinds, including those of inflammatory, vascular and ischaemic origin, and also includes a brief chapter on intra-orbital pathology. There is an introductory account of the neuropathology of brain tumours, with emphasis on classification and neuropathological definitions, more detailed than is found in other imaging textbooks. Introductory chapters also discuss basic principles of computed tomography (CT) and MRI, with emphasis on how to conduct examinations in the context of diagnosing and typing brain tumours. The majority of the book is organized into chapters and sections headed by tumour type; each section consists of a tabulation of the main pathological and generic features of each, a discussion of the findings on computed imaging together with differential diagnosis, and an atlas of examples which in fact comprise the main bulk of the book as a whole.

The text is well written, and the layout is impeccable showing good general consistency from chapter to chapter. The text is brief, and despite the detailed database from which the authors worked, is often surprisingly vague. The authors presumably expect interested readers to consult the extensive tables in the introductory chapters for detail. The illustrations generally demonstrate the range of appearances, but many of the CT images are made on early machines. However, too many of the examples were not histologically proven, but "looked typical" of a given lesion, which seems hardly permissible when, for example, types of glioma were being distinguished.

This book makes a significant contribution to the understanding of brain tumours and their appearances on computed imaging. It can be recommended to specialist readers of this journal. The atlases of both typical and atypical appearances would be of great value to a general radiologist, finding himself with a new CT scanner and relatively little experience in viewing significant intracranial pathology.

J. M. STEVENS

Radiology of Chest Diseases. By S. Lange, pp. ii + 293, 1990 (Georg Thieme Verlag, Stuttgart), DM168.
ISBN 3-13-740701-X

This is a single-author book of moderate size covering all aspects of imaging the chest. Acknowledgment is given to Professor Paul Stark of California for his collaboration and assistance in translating (along with Dr Norman MacLean) from the original German. The virtually faultless anglicization of the text is impressive. The book is divided into three parts: examination technique and normal findings, pulmonary diseases and finally radiological signs and differential diagnosis. The first section deals concisely with normal chest anatomy, and is particularly good in the way it describes the mediastinal stripes and normal segmental anatomy. There is a cursory description of the technical aspects of all the imaging devices brought to bear on the chest, including radionuclide scanning and magnetic resonance imaging (MRI). It is in this section that a computed tomographic (CT) scan of the thorax using double windows (both lung and mediastinal settings in a single image) first appears; this is an unnecessary gimmick that blights most of the remaining CT illustrations. Throughout the book, there are numerous line drawings and diagrams, 381 out of a total of 598 illustrations to be precise. These are elegantly presented and are used to great effect to summarize pictorially the radiological evolution of particular diseases. It is unclear who is responsible for these contributions and they certainly deserve recognition in a future edition. In some of the descriptions of the rarer lung conditions, the pathological terminology is vague and does not tally with either current UK or USA usage. There is a particularly confusing summary of so-called chronic interstitial pneumonia, which lumps together desquamative interstitial pneumonia, bronchiolitis obliterans with organizing pneumonia and giant cell interstitial pneumonia. This is an unsatisfactory account, which is further weakened by an accompanying CT illustration which is used 150 pages earlier to illustrate a case of pulmonary oedema superimposed on emphysema (enterprisingly photographed at different window settings). In fact the coverage of diffuse lung disease, compared with the sections on solid tumours and mediastinal pathology, is the weakest aspect of this book. There are only a moderate number of references listed at the end of the book and a disconcertingly high number are, perhaps not surprisingly, from the German literature. A book of this size cannot hope to compete as a reference source with the third edition of Fraser and Paré's monumental *Diagnosis of Diseases of the Chest*. The slavish adherence to the formula of listing the contribution of each diagnostic test in each disease category becomes tedious; the repetition of "Angiography, Sonography, MRI: no additional information" is striking but hardly enlightening. The last section on the differential diagnosis of a wide range of radiological signs is neatly handled, but results in considerable repetition of the preceding section which covers the individual pulmonary diseases.

In size and intention, this book is similar to the classic but now rapidly ageing Felson's *Chest Roentgenology*. Without the recent appearance of the awesomely authoritative *Imaging of Diseases of the Chest*, by Armstrong, Wilson and Dee, this book could have been safely recommended, but this latest arrival convincingly demolishes such competition.

David M. Hansell

Interventional Radiology. Ed. by R. F. Dondelinger, P. Rossi, J. C. Kurdziel and S. Wallace, pp. xxiv+808, 1990 (Georg Thieme Verlag), DM298.

ISBN 0-86577-286-X

This large multi-author volume edited by Dondelinger, Rossi, Kurdziel and Wallace is a large volume of some 800 pages and more than 1000 illustrations. It is a comprehensive and up-to-date survey of the "state of the art" in a rapidly expanding field. The editorship and authorship are multinational with more than 100 contributors. The names of a large proportion of the contributors are very well known, though, interestingly, not always best known for the subjects on which they are writing in this book.

All the obvious areas of interventional radiology have been covered ranging from biopsies and drainages to the endoscopic and percutaneous management of biliary disease and urinary disease, the whole gamut of therapeutic angiographic techniques and interventional procedures in the digestive tract to percutaneous lysis of the vertebral disc and percutaneous lysis of neural structures. The sections on laser angioplasty and vascular stenting are excellent and reasonably up to date, given the difficulties and time involved in putting together a volume like this. The use of expandable stents is described for the biliary tree and for vascular use. Interestingly, however, though the index appears to be a substantial one, the word "stent" is not to be found in it.

Dipping into this large book for more detailed reading, I did find one or two surprises. For example, neither in the general section on embolization materials nor in the relevant specific sections could I find any warning about the use of sclerosing liquid agents such as alcohol and dextrose in such areas as head and neck, thorax and pelvis. Such a surprising omission is a pity in a book that is otherwise quite strong on indications, contra-indications and complications. However, overall this is a readable, well illustrated and reasonably up-to-date survey of the field. It contains a wealth of detail in most sections on technique, problems and complications and succeeds generally in its stated aim of setting each interventional "problem" in a clear clinical context. It may be recommended to individuals who do a substantial amount of interventional work, and as a good reference book for the departmental library. It is priced at DM298. The fate of the DM and the pound in the near future are not entirely clear to me, but the price of this book in the UK will certainly be more than £100. I must admit I find it very difficult to adjust to the idea of such prices for a book but, as things go these days, especially for books of relatively limited circulation, I would suppose this is value for money.

P. Dawson

Diagnosis of Diseases of the Chest, Vol. III. By Fraser, Paré, Paré, Fraser and Genereux, pp. xxxvi+715, 1989 (W. B. Saunders, Philadelphia), £60.00.

ISBN 0-7216-3872-4

This is one of four volumes dealing with chest disease, and in this third volume, the following diseases are discussed: embolic disease, pulmonary hypertension, airway disease and pneumoconioses.

The book aims to emphasize the value of the chest radiograph in the initial assessment of chest disease. Accordingly, one might anticipate that this book is aimed primarily at radiologists, but this is not so and, given the extensive coverage of the clinical, morphologic and laboratory aspects of disease, many other specialists could have been called upon to give a review.

The book assumes a fairly extensive knowledge of chest disease on the part of the reader, and is targeted at those with both the time and inclination to extend their knowledge of chest radiology. It is not suitable for beginners, and would be inappropriate for registrars trying to do some last minute cramming for exams.

As a radiologist, I found the chapter on pulmonary oedema and thromboembolism rather ponderous, but the chapters on airway disease and pneumoconioses are excellent.

Whilst chest radiograph illustrations are the mainstay of each chapter, there are extensive computed tomography (CT) and isotope examples, illustrations and radiographic images are clear and well described, and are placed within easy access of the relevant text. Each chapter contains a very comprehensive and updated bibliography.

Having read this book one will never dare approach a chest radiograph again with dismissive abandon!

A very thought provoking book which is thoroughly recommended.

J. Hinton

More of Mould's Medical Anecdotes. By R. Mould, pp. xvi+269, 1989 (Adam Hilger, Bristol), £14.95.

ISBN 0-85274-119-7

Dr Mould has done it again. Repeat prescriptions are usually given because the first dose failed; here it is just the opposite, the first was such a success that the patient is crying out for more of the same! Ambrose Bierce defined a prescription as a physician's guess at what will best prolong the situation with least harm to the patient; in this case, any harm will be due to sore ribs from laughter.

There are many delights in this second collection of Mould's Medical Anecdotes, from the first cataract operation in 1000 BC (with an appropriate fine if the operation failed!) to a splendid crop of biological exam howlers, *e.g.* unwanted pregnancy is a sexually transmitted disease (personally, I would have marked that as correct!) There is a delightful essay on Malingering by Richard Asher, with a cautionary tale for all who come to hasty conclusions, and a fascinating sketch of George James Guthrie who had the distinction of passing the MRCS exam at the age of 16. They promptly changed the age at which the exam could be taken to 21.

Anyone who has partaken of Mould's first book of Medical Anecdotes will know what to expect from this collection. If you are not one of those fortunate people, I highly recommend this medicine, the great advantage of which is that you can take large or small doses as often as you like and need never give it up.

N. J. McNally

Bone Tumours. By J. M. Mirra, pp. xvi + 940, 1990 (Lea & Febiger, Philadelphia), £177.42.
ISBN 0-8121-1156-7

It might be thought unusual for a radiologist to be reviewing a two-volume multi-author text on bone tumours for a radiological journal; indeed, in the past there would have been little reason for a publisher to send such a book to this journal. It is now, however, evident that, at least in the field of bone tumour diagnosis and treatment, neither the clinician, pathologist nor radiologist dare work in isolation. The surgeon is often not the practitioner who carries out the initial biopsy, or who decides what to biopsy. The pathologist would be most unwise to come to a diagnosis on the basis of the histology alone. He too must acquire a working knowledge of tumour radiology. The radiologist thus occupies a unique position today in the diagnosis and management of tumours in conjunction with his colleagues, often even perhaps indicating that no biopsy is needed. It is for this reason that a number of textbooks are now available in which the clinical, radiological and pathological features of tumours are integrated, as indeed they are in the clinical context.

This magnificent two-volume textbook is written by an authoritative group. The editor defines one of the aims of this book is "to heighten the awareness of the reader to the importance of skillful interpretation of radiologic data, in particular to the resolution of the final clinico-pathologic diagnosis". Lesions are presented in sequence in terms of clinical findings, skeletal location, radiology, correlation of gross and radiographic analyses of specimens, histology, electron microscopy, differential diagnosis, course, treatment and theoretical considerations. The radiologist is then advised to omit certain chapters, concentrating instead on others.

The book is well produced. Radiographs, xerograms, scintigrams, computed tomography (CT) and nuclear resonance (NR) images are all used, nicely illustrated and well described. The amount of information contained in these two volumes is obviously vast, with all you would ever want to know about bone tumours down to the most obscure sub-type. The references are plentiful, and the text is easily readable, though often a little anecdotal.

Who, then, should buy this excellent textbook of osteopathology which has a multidisciplinary slant? It should be found in X-ray departments wherever bone tumours are seen, diagnosed and treated, which in practice means in larger centres, often associated with a bone tumour registry. The price of these volumes is not excessive for such a major work.

Peter Renton

Exercises in Diagnostic Imaging. By C. J. Garvey, G. H. Whitehouse and R. M. Mendelson, pp. ii + 170, 1989 (Butterworths Scientific Ltd, Guildford), £12.95.
ISBN 0-407-00601-X

This book is the latest in a long line of self-assessment books primarily aimed at MRCP candidates. The preface indicates that it is the authors', and obviously the publisher's, hope that this book will find favour with others including trainee radiologists. The requirements and standards of MRCP and FRCR are quite different, and the level of difficulty of the cases included are more appropriate to the membership candidate. Nevertheless, radiologists of all ages and persuasions could have a happy and instructive time leafing through this book.

It has been said that the "instant", basically pictorial monograph, is an attractive proposition for would-be authors because it is relatively quick to devise. In this collection it is obvious that the radiographs have, for once, been painstakingly selected so that the abnormalities can be seen on the printed page rather than imagined. The clinical information accompanying each illustration is minimal, in keeping with the MRCP format, and only very rarely do the clinical details give the game away. The questions in each case are varied and do not lapse into the usual and monotonous "what is the likely diagnosis?". The cases encompass a wide range of techniques which might appear in the MRCP and these include, amongst plain radiographs which easily make up the majority, nuclear medicine studies and a single cranial magnetic resonance imaging scan. The great strength of this book is the pragmatic discussion which follows each answer, notably the appropriateness of imaging tests to various clinical problems. There are no glaring errors, but a pneumatic sedimentation rate caught my eye: an erythrocyte sedimentation rate is given as 80 mm Hg. There is an insatiable demand for this type of book, which makes it almost impossible to saturate this particular market. At £12.95, this collection is reasonable value and deserves, but probably does not need, recommendation.

David M. Hansell

Laser Angioplasty. Ed. by Timothy A. Sanborn, pp. xi + 121, 1989 (Alan R. Liss Inc, New York), £49.50.
ISBN 0-471-50992-2

This book is an introduction to the clinical use of lasers in cardiovascular disease. It is, however, devoted almost entirely to one type of laser device, the metal-tipped laser probe, although a brief last chapter describes alternative devices for delivering laser energy to atherosclerotic plaques. The use of lasers for ablation of atheroma is still experimental, but it is a rapidly developing field. As a consequence, much of this book is inevitably already out of date; other parts of the book are intentionally historical, as the early attempts at using laser energy in arteries are described.

Multi-author books often suffer from wide variations in the value of individual chapters, and this book is no exception. There are two excellent chapters which contain much useful information on techniques of laser angioplasty, one by David Cumberland et al, from Sheffield and the San Francisco Heart Institute, and the other by Richard Leachman from the Texas Heart Institute. Any radiologist who is starting to perform laser angioplasty with the laser probe should read these two chapters. On the other hand, a complete chapter is devoted to basic techniques of peripheral angioplasty; in the UK it would be unimaginable for any radiologist to attempt a laser angioplasty without wide experience of conventional techniques.

The book is therefore neither a simple overview of the subject for the uninformed nor a detailed technical manual for the experienced radiologist. This book is more suited to the United States market where, as it is admitted in the Foreword, media "hype" and marketing pressure is causing hospital administrators to persuade radiologists and cardiologists to instal and use lasers that their hospital may be first in the field and thus increase their occupancy. This book will be of strictly limited value in the UK where such pressures do not exist. In the present economic climate, few hospitals will install and use laser devices for peripheral or coronary angioplasty until their advantages are more fully proven. Radiologists who are interested in the subject would be better advised to read the excellent editorial in *Clinical Radiology* (February 1990) by Anna-Marie Belli and David Cumberland; taken in conjunction with their listed references, this will provide a more informed overview than is available in this book.

MIKE DEAN

Fluorescein Angiography. Textbook and Atlas. By Gisbert Richard, pp. viii + 236, 1990 (Thieme Medical Publishers, Stuttgart), DM198.
ISBN 0-86577-336-X

This book is a nicely prepared one, most of the illustrations coming from the University of Mainz in Germany. It is not clear whom the book is aimed at, but it is most likely for junior ophthalmologists during their residency training.

There are introductory pages about fluorescein, its use, the evaluation of angiograms and the appearance of normal retina and choroid. There is a short section at the end about complications of fluorescein injection and their management. The text was originally written in German and then translated, which results in a text difficult to read, with sentence structures left in their heavy Germanistic style. There are a few sentences that make little sense, *e.g.* on page 11: "an embolus may occur singular or may be found in various segments of the vasculature." Instead of using well known terms such as saccadic movement, they use "physiologic minimal motions", a confusing term. Even chapter titles are not quite correct, *e.g.* "Disturbance of venous retinal circulation" instead of retinal venous circulation. In some of the sections abbreviations or letters in equations are not explained.

In addition, quite a lot is made of videoangiography, but at no time is it indicated how this helps in evaluating angiograms. Other recent advances are not mentioned, such as the use of the scanning ophthalmoscope with fluorescein.

Coming to the text and illustrations: the essential part of the book. The angiograms on the whole are of high quality, though capillary detail is rarely demonstrated, and magnification of small areas to show this would have been welcome. The illustrations are all in black and white, while colour photographs would have been an advantage. In some instances we have to imagine what is described. More important is the lack of stereo photographs, which would have clarified much of the text, and which is essential for interpretation of angiograms.

The text covers most conditions, but there are some poorly described and a few conspicuous by their absence. It is amazing that Sickle cell retinopathy is not mentioned, and that AIDS is not fully described, except as a cause of cytomegalovirus infection. In the section on venous occlusion, central vein occlusion is not shown, nor is the difference between ischaemic and oedematous vein occlusion demonstrated. While treatment is mentioned in the majority of conditions, Fig. 5.14 demonstrates diabetic retinopathy with new vessels on the disc, and large peripheral (lateral to the macula) area of non perfusion. At no time is it mentioned that this area should be treated. The different types of maculopathy in diabetes are not mentioned, which is a sad omission, as they have different prognoses.

The section on the macula is probably the best of all the sections, and even though it suffers from a lack of stereo photographs it is clear with excellent illustrations.

The first book on fluorescein angiography was by Wessing, now some 20 years ago. A full update, easily readable would have been welcome. This is not it.

EVA M. KOHNER

BIR Bulletin

Honorary Editor, BIR Bulletin: D. Rickards, LRCP, MRCS, FFR(D)SA, FRCR
Please address all correspondence to: Honorary Editor, BIR Bulletin, The British Institute of Radiology,
36 Portland Place, London W1N 4AT
The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

Radiology &
Oncology '91

Brighton, 29 April - 1 May 1991

Who is writing the history of radiology?

The science of making X-ray images is 96 years old this year, old enough to have a respectable history behind it. Who is writing this history? The centenary approaches and all manner of books and articles will appear. Many will be written by journalists with little or no first hand knowledge of the subject. In the absence of information from us, professional radiologists, radiographers and medical physicists, all manner of nonsense will be written. And our permission will not be requested first.

We have now a well written chronology of the first 30 years of British diagnostic radiology. We also have a picture book, and the promise of another volume by the same author. Recently a detailed scientific account of the development of tomography has been published. There have been three accounts of radiology written by Americans, none of them recent. The French have recently produced a praiseworthy volume covering worldwide themes as well as their national radiological history.

We still lack a critical, analytical examination of the way in which our discipline and the professions have developed from the clinical and historical viewpoint. Some aspects of radiological history can be very well dealt with by engineers, physicists and social historians, but there are many topics which only radiographers and radiologists can handle.

There are any number of different problems experienced by our professional forbears which need exploration. How, for example, was the barium meal developed? When radiologists ceased to be both diagnostic and therapeutic, did they regret losing part of their role? What has been the link between pharmaceutical manufacturers of contrast media and the doctors who used them? If the development of MRI depended on technology derived from CT, has there been any contribution in the other direction? How has the imaging profession divided itself into its medical and non-medical members, and is this pattern changing?

We shall not be attempting to deal with all these momentous issues in one short session at the Brighton Congress, but you will have a little foretaste of the delights awaiting you at the Joint British Centenary Congress in 1995. You can hear short lectures on the history of early radiographic apparatus, angiography and tomography, each given by experts in those fields, and you will have the opportunity to ask questions. It is also planned to have a few historical radiological exhibits on show. I hope that some of you will be inspired to research and write on the history of radiology yourselves.

J. M. GUY
YEOVIL DISTRICT HOSPITAL

Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.

Cracking gallbladder and bile duct problems

A report on the meeting by Dr Mary E. Roddie

Senior Registrar in Radiology, Hammersmith Hospital

The treatment of gallstones and bile duct stones has changed dramatically in the last few years. In order to inform physicians, surgeons and radiologists involved in this clinical area of the latest developments, a one-day meeting was held at the BIR on 18 October, 1990. Philips Medical Systems generously supported the meeting and over fifty delegates from all over Britain attended. An international flavour was added by two delegates from Australia, a further delegate from Jerusalem and, of course, the presence of Peter Mueller who had come all the way from Boston to talk about extracorporeal shockwave lithotripsy (ESWL). Peter Mueller is one of today's leading hepatobiliary interventional radiologists and having travelled the longest distance to attend the meeting was the "guest of honour". However, the other seven "home-grown" speakers were no less eminent and consisted of medical, surgical and radiological experts in the field of gallbladder and bile duct stones, several of whom had played an important role in the development of the techniques they were talking about. Julian Walters from Hammersmith Hospital is a gastroenterologist with a particular interest in oral gallstone dissolution. Chris Russell from Middlesex Hospital is a hepatopancreaticobiliary surgeon who has been adopting the newer surgical techniques of mini-cholecystectomy and laparoscopic cholecystectomy with enthusiasm and in collaboration with his radiological colleague, Bill Lees, has gained a large experience of percutaneous cholecystolithotomy (PCCL). Irving Benjamin, who will soon be leaving Hammersmith Hospital to take up the Chair of Surgery at King's College Hospital, is probably one of the most experienced hepatobiliary surgeons in Britain with particular expertise in surgery for cholangiocarcinoma. The radiologist speakers (Bill Lees from Middlesex Hospital, Derrick Martin from Withington Hospital, Manchester, Bob Dick from The Royal Free and Andy Adam from Hammersmith Hospital) are all well known for interventional hepatobiliary radiology and need no further introduction to the readers of this journal!

After registration and coffee, when the delegates and speakers had the chance to meet each other, the scientific meeting began with Andy Adam chairing the first session. The first talk, by Julian Walters, dealt with the technique of oral gallstone dissolution. We were reminded of just how common gallstones are (it is estimated that 15–20 million Americans have gallstones). Oral dissolution is an attractive method in that it is an extremely safe, outpatient treatment. Unfortunately it is limited to small, cholesterol gallstones and he estimates that only 5–10% of patients will satisfy the criteria for this technique. For those patients who are suitable, a combination of ursodeoxycholic acid and chenodeoxycholic acid appears to give the best dissolution rate with fewest side effects. There was a lively discussion after this talk on the subject of whether patients for oral dissolution should be assessed by oral cholecystography or ultrasound. The radiologists in the audience felt strongly that ultrasound provides all the required information but the physicians and surgeons argued that the information they need, such as the exact number and size of the stones, is often poorly documented in the ultrasonographer's report. This led to the counter argument by the radiologists that, in most cases, the information is not recorded because the clinical information is inadequate. The answer seems to be to aim for better communication between radiologists and referring clinicians!

Chris Russell's lecture gave a fascinating insight into how the surgeons are responding to the threat of physicians and radiologists venturing into the field of gallstone therapy. The most impressive of the new surgical techniques is laparoscopic cholecystectomy which can be performed through four tiny incisions and allows the patient to leave hospital as early as two days post-operatively. The surgical technique, however, is very technically demanding and in these early days generally takes up to twice the time of a conventional cholecystectomy. An alternative is the "mini" cholecystectomy, performed through a 4–5 cm incision with specially adapted long-handled instruments. This is an easier operation for the surgeon and the patient still leaves hospital early, on the second to fourth post-operative day. Whether these techniques will result in an increased rate of accidental common bile duct injury is impossible to say at present, but the Middlesex patients are being meticulously followed up with this complication in mind. Chris Russell wound up his talk with the prediction that in 10 years time 75% of patients will have their gallstones treated by the newer surgical techniques or PCCL.

The floor was then taken by Peter Mueller who discussed the rise and fall of ESWL. The technique appeared to peak in popularity in 1989 but it has since fallen from favour with very few new machines being purchased in 1990. In America, this can be explained by a combination of factors. First, the Food and Drugs Administration failed to grant approval for the technique; secondly, the USA results were disappointing compared with those published from European centres; finally (but perhaps most importantly!) an unfavourable article on ESWL with a strongly negative headline was published in The Wall Street Journal. On a more serious note, Peter Mueller pointed out trans-Atlantic differences in technique which may explain the striking difference in results. The Europeans generally use a higher kV and allow a larger number of shocks per patient and this may be important. It is also notable that in America targeting of the stones is usually performed by non-radiologists. The conclusion seems to be that there is a definite role for ESWL in the management of gallstones but that it is very much smaller than was first imagined.

Bill Lees was the final speaker of the morning session and described his experience with MTBE, delivered into the gallbladder via a percutaneous, transhepatic catheter in eleven patients over the course of one year and achieved a completely successful result in only one of these and he has now, not surprisingly, abandoned the technique. The results for his first hundred PCCL patients, however, are very impressive with a success rate of 95% and this is obviously an important new technique. Practically any patient with gallstones is eligible for PCCL as, unlike oral dissolution and contact dissolution, gallstones of any size, number and composition can be treated.

A panel discussion with all the morning's speakers concluded the first session. Points raised included the risks of carcinoma developing if the gallbladder is retained after stone removal. This was answered by Chris Russell who stated that this risk is, in fact, very small and that the main risk to the patient if the gallbladder is not removed is that the gallstones will recur. Radiologists in the audience wanted to know whether PCCL should be performed in most hospitals or whether it should be confined to a few specialist centres. Bill Lees replied that the technique must be learnt by apprenticeship and that about twelve procedures should be performed before a radiologist can feel comfortable with the technique (*i.e.* a longer learning curve than most interventional radiological procedures). However, he concluded that, providing a good working relationship exists between surgeons and radiologists, there seems to be no reason why the technique should be confined to specialist centres. The final question put to the panel by Andy Adam was one we all wanted to ask: how would each of the panel have their gallstones treated? Interestingly, all the panelists opted for mini cholecystectomy, although Julian Walters said he would try oral dissolution first if his gallstones were non-calcified, and both radiologists said that they would consider PCCL if they were unfit for surgery.

After lunch the afternoon session began with Bob Dick in the chair. Derrick Martin started the session by presenting some of the newer endoscopic approaches to the removal of bile duct stones. As in other areas of interventional radiology, recent additions and refinements to the endoscopists "tool box" have undoubtedly increased the success rate of this technique. These include the needle knife as an alternative to the bow sphinctertome, wire-guided sphinctertomes, mother-and-baby endoscopes and choledochoscopes. One of the main causes of endoscopic failure is large stones but the advent of the mechanical lithotripter, which literally crushes large stones, has partly solved this problem. Derrick Martin has found MTBE infusion via a per-nasal catheter useful in a small number of patients and has also found ESWL helpful in fragmenting bile duct stones; it was interesting to hear that after ESWL most patients still require endoscopic removal of the fragments.

The second speaker of the afternoon was the Chairman, Bob Dick, who talked about percutaneous and combined approaches to common bile duct and intrahepatic stones. The Burhenne technique for removing retained bile duct stones via a T-tube tract after cholecystectomy is a well established technique so his lecture concentrated on the more technically demanding subject of intrahepatic stones. He has had a large experience in dealing not only with hepatic stones, but with the benign bile duct strictures which predispose to stone formation. This type of patient poses one of the greatest challenges to both the surgeon and the interventional radiologist. Although the percutaneous, transhepatic route can be used (and this was illustrated beautifully by many of Bob Dick's own cases) he emphasized the advantage of a surgically fashioned access loop to allow retrograde access to the biliary tree in difficult cases.

This subject was touched on by Irving Benjamin in his excellent talk on surgical options in bile duct cancer in the context of patients who have undergone hepaticojejunostomy for cholangiocarcinoma. This group may also develop anastomotic strictures and whether these are benign or malignant in nature, retrograde access for the radiologist may prove invaluable in both cases. Curative resection is, unfortunately, available to only a small group of patients with this disease but interestingly, patients having undergone resection seem to have a better quality of life than those having had a simple bypass operation. The results of liver transplantation, disappointingly, seem to be poor and there is, to date, no convincing evidence that internal radiotherapy with iridium wires placed within the ducts has a significant beneficial effect.

Andy Adam was the final speaker of the day and he discussed recent advances in the radiological management of malignant obstructive jaundice. He pointed out that palliation with biliary endoprostheses is preferable to external drainage in these patients because even if they block (which plastic stents inevitably do) they can easily be replaced. The advent of self-expanding metallic stents, however, has revolutionized the treatment of patients with cholangiocarcinoma as a wide internal diameter stent can now be inserted over a small (7 French) delivery catheter which seems to have significantly reduced the procedure related mortality of percutaneous stent placement.

A panel discussion ended the meeting. Points raised included the question of whether a stent should be inserted if stones are left in the common bile duct after an attempt at endoscopic removal. Opinion was divided into those who felt that a stent helps to break up retained stones and those who felt that the presence of a stent hinders the stones from dropping out. The question of whether benign strictures should ever be stented was raised and the opinion of the panel was that, although there was a place for stent placement in benign disease, it should generally only be performed as a last resort.

The meeting was then closed and the opinion of those who attended (including the speakers) as they disappeared round the corner of the British Institute of Radiology towards the nearest hostelry was that they had been well and truly updated on this fascinating and rapidly changing subject.

The proceedings of this meeting can be found on pages 187–188 of this issue of BJR

Nycomed Scandinavian Scholarships 1991

The selection committee had a very difficult choice this year. There were eight excellent applicants, all of whom had submitted detailed applications and for any one of whom considerable benefit would accrue from their proposed visits. All would have made excellent ambassadors for British radiology.

On the basis that just over £12 000 was available to the BIR, they decided to offer three scholarships of £4000 each.

The successful candidates were Dr T. S. Creasy, Senior Registrar, Oxford to visit three centres in Copenhagen; Dr D. G. Hughes, Senior Registrar, Manchester Royal Infirmary (recently appointed Consultant Neuroradiologist, Hope Hospital, Salford), to visit Gothenburg; and Dr John Rawlinson, Senior Registrar, Southampton (recently appointed Consultant, Gateshead), to visit Lund and Arhus.

The BIR are grateful to Nycomed for such generous support.

Library

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays and Thursdays).

The journal stock includes more than 100 titles. Although journals may not be taken out of the library, there is a photocopy service, also available by post or Fax. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

Members can apply to the BIR librarian for a visitor's card which allows limited use of the RSM library for reference purposes, including photocopying and searches.

Lecture, Conference and Meeting Facilities

Available for use at 36 Portland Place,
London W1

The BIR lecture Theatre, with raked seating and extensive audiovisual equipment, accomodates 100 people in air conditioned comfort.

The conference room accommodates a maximum of 34 people with modular furniture which can be arranged to suit the needs of individual users.

For further information please contact the House Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

BIR Calendar

Unless otherwise indicated, enquiries about the following events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-580 4085).

Radiation Oncology/IPSM
April 10, 1991
All day meeting organized by IPSM

RADIOLOGY AND ONCOLOGY 91 and MED X RAY
29 April–1 May
Metropole Hotel, Brighton
Speakers:
3M Mayneord Memorial Lecture:
Prof. S. Dische
Silvanus Thompson Memorial Lecture:
Dr R. Berry
Presidential Address:
Prof. C. A. Joslin
Mackenzie Davidson Memorial Lecture:
Prof. S. Dische

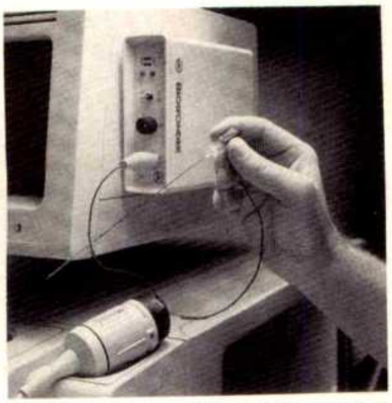
Radiation Oncology and Radiobiology: Particle Therapy
June 7, 1991
Organizer: Dr R. D. Errington
Speakers: Dr D. Bewley, Dr N. McNally, Prof. G. W. Griffin, Mr J. Hungerford, Dr T. Bates, Dr S. Gore and Prof. J. M. Slater

The New Legislation — Friend or Foe (After the White Paper ... and into Europe)
June 13, 1991
All day meeting orginized by the Industry Committee
Chairmen: Prof. C. A. Joslin, Dr O. Craig and Miss D. Rigg
Speakers include Dr J. Roylance, Dr I. Watt, Mr E. Sutherland, Prof. I. Isherwood and Mr P. Richardson

Conversazione
June 27, 1991
Painter's Hall, London
Lecture: " Half an Eye on the Sky", by Sir Stephen Furness.

Industry News

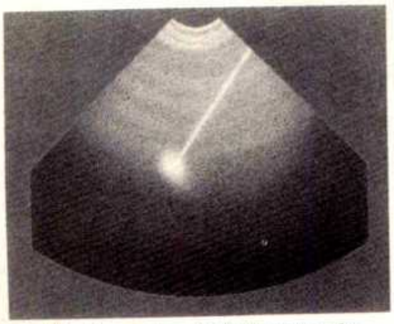
ATL's approach to needle tip visualization



The Biosponder needle-tip guidance module with biopsy/aspiration needle.

ATL's Biosponder needle tip guidance nodule offers a revolutionary approach to ultrasound-guided biopsy/aspiration procedures. With a beeping tone and a flashing marker, the module provides a continuous beacon for easily locating the tip of the biopsy needle.

A common fine-guage biopsy/aspiration needle is advanced through the tissue. Inserted into it is a special stylet with an integral transponder sensor. A signal cable connects it to the module. When intersecting the image plane, the sensor confirms the needle tip position by displaying a small bright marker at its corresponding location on the image. An audible tone verifies that the tip is within the image scan beam. As needed, the module can be moved for use with another Ultramark 9 System.



The Biosponder clearly indicates the position of the needle tip.

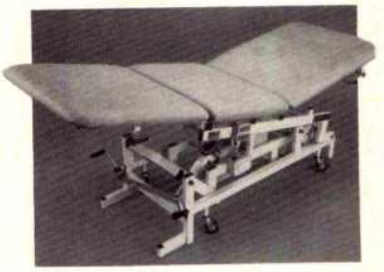
UK's 100th 3M Laser imager system goes to Oxford

3M have announced that the number of laser imagers in the UK has reached one hundred with the installation of the system in the new MRI centre at the John Radcliffe Hospital, Oxford. Here it interfaces with an IGE Signa MR Scanner for the ideal scanning of patients. There are now three 3M laser imagers in Oxford linked to a CT Pace Scanner and a Sytec '3000' scanner, also supplied by IGE.

Dr Stephen Golding, Clinical Director of the Oxford MRI centre, explained that the system will be examining patients for suspected brain tumours, diseases of the central nervous system, disorders of the spine, chest and abdomen, as well as the ear, nose and throat. It will also be used for clinical research into relevant specialties like cardiac ailments, multiple sclerosis and others.

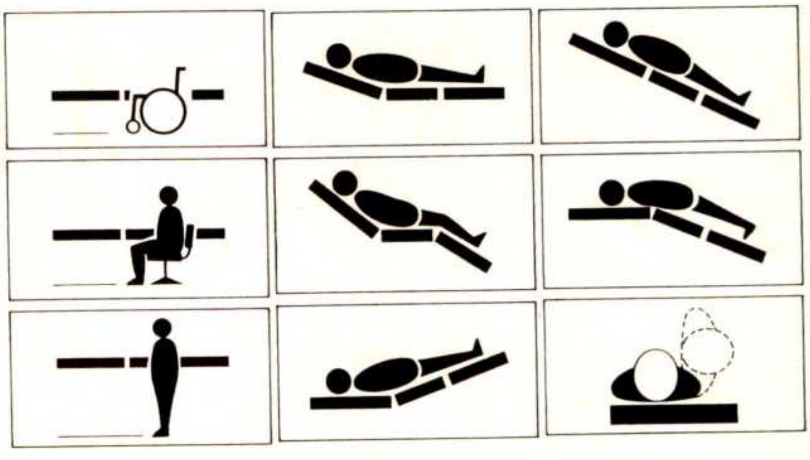
For further information contact Chris Varian, Medical Imaging Systems Group, 3M United Kingdom plc, 3M House, PO Box 1, Bracknell, Berkshire RG12 1JU. Tel: 0344 58799.

Autotilt ultrasound couch



The Autotilt 20 couch has been designed for optimum patient positioning across the full range of ultrasound examinations. It is powered by two electrically operated fail-safe motors and controlled by a twin airline handswitch. Finger-tip controls enable both the height and tilting angle to be adjusted easily and quickly, even during scanning. The wide three-section plinth with a raising back-rest and adjustable foot section ensure that the patient is both safe and comfortable. Fully retractable wheels operated by a single action lever allows for a smooth change from stationary to mobile mode.

For further information contact Knight Imaging, Old School House, South Street, West Tarring, Worthing, West Sussex BN14 7NL.



BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £275 p.a. member companies are offered an attractive benefits package.

To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

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Tel. 071-352 8051. Fax: 071-376 4508.
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Contact Betsy Riley, Managing Director.

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Tel. 0296 395222.
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Contact Mr James McLaughlin, Sales and Marketing Manager.

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Tel. 0925 835022.
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Tel. 081-954 2366.
Product areas 3, 6.
Contatct Mr Dennis Lewis, Sales Manager.

Cardiac Services Ltd
95A Finaghy Road, South Belfast BT10 OBY. Tel. 0232-625566.
Product areas 1, 3, 4, 5, 6.
Contact Mr R. J. Brown. Managing Director.

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Meetings and Courses

As a service to our readers, notice of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR Bulletin.

Principles and Practice of Clinical MRI
February 28–March 5, 1991
Florida, USA
Further details: Program Coordinator,The Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205. Tel: (301) 955-2959.

Clinical Oncology Symposium: Challenges Brachytherapy
8 March, 1991
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London, W1N 3DG. Tel: 071 - 636 4432. Fax: 071 - 323 3100.

Breast Imaging Update
March 16–18, 1991
California, USA
Further details: UCSF School of Medicine, Radiology Postgraduate Education, Box 0628, Room C-324, San Francisco, CA 94143-0628, USA. Tel: (415) 476-5731. Fax: (415) 476-9213.

23rd International Diagnostic Course
April 6–13, 1991
Davos, Switzerland
Further details: Medical Congress Management, PO Box 2, CH-8029, Zürich, Switzerland. Tel: (01) 255 19 15. Fax: (01) 261 05 78.

The London/Bart's FRCR Part 1 — Revision Course
April 11–12, 1991
London
Further details: Dr P. Butler, Department of Neuroradiology, The Royal London Hospital, Whitechapel, London E1 1BB. Tel: 071-377 7164.

ANGIO 91
April 12–14, 1991
Paris, France
Further details: Angio 91 Scientific Committee, Doctor Philippe Caillard, 3 place des Vosges, 75004 Paris, France. Tel: (1) 42 74 64 64. Fax: (1) 40 29 04 51.

8th Annual Congress of the European Socity of Magnetic Resonance in Medicine and Biology
Zürich, Switzerland
Further details: Medical Congress Management, PO Box 2, CH-8029, Zürich, Switzerland. Tel: (01) 255 19 15. Fax: (01) 261 05 78.

Postgraduate course on Medical Oncology
April 21–27, 1991
Amsterdam, The Netherlands
Further details: CCCA, c/o Mr R F M van Bokhoven, Plesmanlaan 125, 1066 CX Amsterdam, The Netherlands. Tel: (31) 20-172903. Fax: (31) 20-155904.

The Management of Spent Nuclear Fuel
April 29–30, 1991
London
Further detals: Liz Hide, IBC Technical Services Ltd, Bath House (3rd Floor), 56 Holborn Viaduct, London EC1A 2EX. Tel: 071-236 4080. Fax: 071-489 0849.

Radiology and Oncology 91
April 29–May 1, 1991
Brighton
Further details: The Conference Office, The British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

Blood Vessel Imaging using Ultrasound Techniques
May 8–10, 1991
Devon
Further details: Mr K. N. Humphries, Blood Vessel Imaging Course, 10 Swale Drive, Chandlers Ford, Hampshire, SO5 3QY.

Recomendations of the International Commission on Radiological Protection
May 9–10, 1991
London
Further details: Katie Lye, IBC Technical Services Ltd, Bath House (3rd Floor), 56 Holborn Viaduct, London, EC1A 2EX, Tel: 071-236 4081. Fax: 071-489 0849.

G.RA.D.O.4, International Meeting on Oncologic Imaging on Endocrine Glands Tumours
May 9–10, 1991
Rome, Italy
Further details: Luigi Tipaldi, Istituto Regina Elena, Radiologia e diagnostica per immagini, Viale Regina Elena, 291 00161 Roma, Italia. Tel: (06) 4985207. Fax: (06) 4452337. Abstracts Deadline: January 31 1991.

Joint Meeting of the Cardiovascular and Interventional Radiological Society of Europe
May 13–16, 1991
Oslo, Norway
Further details: Medical Congress Management, PO Box 2, CH-8029, Zürich, Switzerland. Tel: (01) 255 19 15. Fax: (01) 261 05 78.

10th International Conference on Laser Spectroscopy
June 17–21, 1991
Font-Romeu, France
Further details: Professor M. Ducloy, Laboratoire de Physique des Lasers, Universite Paris-Nord, F-93430 Villetaneuse, France.

Second European Summer School on Radiological Protection
July 8–12, 1991
Cambridge
Further details: Liz Hide, IBC Technical Services Ltd, Bath House (3rd Floor), 56 Holborn Viaduct, London EC1A 2EX. Tel: 071-236 4080. Fax: 071-489 0849.

2nd International Workshop on Auger Spectroscopy and Electronic Structure
September 4–6, 1991
Lund, Sweden
Further details: Professor C O Almbladh, Department of Theoretical Physics, Lund University, Solvegatan 14A, S-22362 Lund, Sweden.

XIIIth International Congress of Lymphology
September 29–October 5, 1991
Paris, France
Further details: Medical Congress Management, PO Box 2, CH-8029, Zürich, Switzerland. Tel: (01) 255 19 15. Fax: (01) 261 05 78.

XIIth International Congress of Head and Neck Radiology
October 6–9, 1991
Zürich, Switzerland
Further details: Medical Congress Management, PO Box 2, CH-8029, Zürich, Switzerland. Tel: (01) 255 19 15. Fax: (01) 261 05 78.

XVIIth Congress of the European Society of Neuroradiology
October 8–12, 1991
Zürich, Switzerland
Further details: Medical Congress Management, PO Box 2, CH-8029, Zürich, Switzerland. Tel: (01) 255 19 15. Fax: (01) 261 05 78.

Fundamental Basis: Do Breast Microcalcifications have a specific Ultra-Structure?
October 9, 1991
France
Further details: M. J. Rodiere, Institut D'Imagerie Medicale, Miniparc - Bat 2, Rue de la Croix Verte, 34090 Montpellier, France.

Current Research in Osteoporosis and Bone Mineral Measurement

Editor:

E F J Ring, Royal National Hospital for Rheumatic Diseases, Bath, UK

The study of osteoporosis has received a great deal of momentum in the last few years. This is partly due to the emerging technology for *in vivo* bone mineral measurement.

A variety of quantitative methods have come into clinical use, based on single and dual photon absorptiometry, computed tomography and broad band ultrasonic attenuation. The 95 papers reported here give authentic coverage of the practical issues which affect the clinical use and interpretation of *in vivo* densitometry. In the section relating to Clinical Studies, a good cross-section of practical problems is addressed, and this indicates the growing interest in this field of medicine. The search for pharmaceutical treatments which will slow down or even attempt to reverse the natural bone loss process is also reported. An interdisciplinary forum of scientists, bioengineers and clinicians has contributed to this publication.

June 1990 96 pages 266 x 196 mm Softcover
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The Toronto-Bayview Regional Cancer Centre, an Ambulatory Care Centre, administered by the Ontario Cancer Treatment and Research Foundation, is an integral part of Sunnybrook Health Science Centre, which includes an inpatient cancer unit for patients under the care of radiation, medical and gynecological oncologists. The surgical staff participate in multidisciplinary site specific clinics. At present there are nine medical oncologists and three gynecological oncologists on the full time Cancer Centre staff. Adjacent to the Cancer Centre is the newly opened Reichmann Research Institute, which includes a Division of Cancer Research. The University of Toronto has a single Postgraduate Training Program in radiation oncology, with rotation of residents between the two University Cancer Centres.

This position requires a mid–career radiation oncologist with an established academic record, who will be eligible for a Full or Associate Professorial appointment within the Univeristy of Toronto's proposed Department of Radiation Oncology. The principal task for the successful candidate will be the creation of a major academic radiation oncology resource. In accordance with Canadian immigration requirements, this advertisement is directed initially to Canadian citizens and permanent residents.

If this is the right challenge for you send a summary letter and curriculum vitae to:
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Toronto-Bayview Regional Cancer Centre, 2075 Bayview Avenue, Toronto Ontario, M4N 3M5.

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Radionuclides in Brachytherapy: Radium and After

(BJR Supplement No. 21)

Editor

N G Trott, Emeritus Reader in Physics as applied to Medicine, University of London, UK

This report, prepared by a multidisciplinary working party set up by the British Institute of Radiology, reviews the clinical, radiobiological and practical aspects of brachytherapy using gamma and X-rays emitted by both natural and artificial radionuclides.
Radionuclides in Brachytherapy is a comprehensive introduction to the current state of the subject, as well as giving the background to the changes in techniques that have taken place in the last 40 years. Including tables, illustrations, a glossary and outline of ICRU and BCRU recommendations plus a helpful list of manufacturers and suppliers, this report will be indispensable for anyone involved in theoretical or practical aspects of radiobiology or dosimetry using this method of treatment.

".... a document that should be read by every physicist and radiotherapist concerned with brachytherapy."

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HPA Bulletin

January 1988 54 pages 266x196 mm Softcover
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NEW **From the British Medical Ultrasound Society, published by the British Institute of Radiology**

CLINICAL APPLICATIONS OF

ULTRASONIC FETAL MEASUREMENTS

By **Tony Evans, Pat Farrant, Maureen Gowland, Margaret McNay and Bernard Richards**

This booklet is the Final Report of the BMUS Fetal Measurements Working Party, set up by BMUS in 1986 to advise on the choice of Tables and Techniques for routine use by sonographers.

The literature abounds with Tables of Values of a large number of anatomical measurements which can be performed at various stages of pregnancy. In many cases, there is disagreement between authors and it is difficult to choose the optimum combination of measurements and the optimum circumstances in which to use them.

The booklet provides advice on these topics based on a careful study of the published data and taking into account the statistics of each published series. The report identifies THREE specific tables for routine gestational age assessment and THREE for monitoring growth as well as TWO for fetal weight estimation. For each measurement discussed a description of the best technique is provided along with a Graph, Table of Values and, in most cases, a formula.

This will be of value to all sonographers involved in routine ultrasound studies of fetal development and provides guidance in the confusion which currently exists because of the multiplicity of data in use in different hospitals.

CLINICAL APPLICATIONS OF ULTRASONIC FETAL MEASUREMENTS

November 1990, 30pp, 297 x 210mm, Softcover, *0-905749-24-3*, Illustrated

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Madison WI 53706, USA. Fax: 608 262 2413 for dollar price.

Technical and Physical Parameters for Quality Assurance in Medical Diagnostic Radiology

Tolerances, limiting values and appropriate measuring methods.
(BIR Report 18)

Editors
B M Moores, Christie Hospital and Holt Radium Institute,
Manchester, UK
F E Stieve, Institut fur Strahlenschutz, Neuherberg, FRG
H Eriskat, Commission of the European Communities, Luxembourg
H Schibilla, Commission of the European Communities, Brussels

Quality assurance is becoming more widely implemented within diagnostic radiology. Its objective is that radiological examinations provide satisfactory and consistent information while keeping exposure to the patient as low as is reasonably achievable. To attain this objective, high performance of the radiological equipment and the image processing must be maintained, which in turn requires specific control of the associated technical and physical parameters.
This volume is the edited proceedings of a workshop organised by the Commission of the European Communities. The workshop was wide ranging in its discussion of instrumentation, measuring methods and techniques of quality control, as well as their tolerances.
The limiting values of the relevant parameters were described and submitted for possible agreement with a view to proposing their standardisation.
Radiologists, radiographers, medical physicists, manufacturers of X-ray equipment and regulatory bodies, whether developing new quality assurance programmes, or reviewing existing ones, or deciding about technological improvements or health care and radiation protection investments will find this book a useful reference.

February 1989 166 pages 266x196mm Softcover
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Megavoltage Radiotherapy 1937 –1987

(BJR Supplement No. 22)

Editors
P N Plowman and **A N Harnett**
Both at St. Bartholomew's Hospital, London, UK

Megavoltage Radiotherapy 1937 – 1987 is the proceedings of a conference held to mark the 50th anniversary of megavoltage radiotherapy at St. Bartholomew's Hospital and contains 15 full papers from invited speakers and over 100 abstracts. It is a significant reference work on current practice in radiotherapy, whilst offering insights on future trends as well – a vital publication for clinicians and all those involved in cancer management.

> *"This collection mirrors the interests of the many past and present associates of this well-known institution, and will be of interest to radiotherapists, physicists and radiobiologists"*
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> *International Journal of Radiation Biology*

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Assurance of Quality in the Diagnostic X-Ray Department

The report of the BIR Diagnostic Methods Committee

Editors

J A Garrett, Director of Medical Equipment Management Organisation, Bristol & Weston Heath Authority, UK
D Gifford, Deputy Chief Physicist, Frenchay & Southmead Health Authorities, UK
M J Harvey, Middlesex Hospital, London, UK
P Goddard, Consultant Radiologist, Bristol Royal Infirmary, UK

Producing images, whether photographically or in electronic form, is the primary purpose of the diagnostic radiology department.

As the range of imaging modalities increases and the equipment for each becomes more sophisticated, awareness is growing of the necessity to review and assess the quality of the imaging process. While there are many interdependent factors that may affect image quality, each may in many cases be assessed by quite simple tests. As well as addressing the organisational, economic and human factors, which are a vital part of the imaging process, this handbook represents a wide range of well-tried tests suitable for use in both small and large X-ray departments.

The second section of the book presents the wider systems approach to quality assurance with reference to recent standards for QA and how these may be applied to diagnostic radiology.

The final part discusses quality assurance in computer assisted imaging, computed tomography, magnetic resonance imaging, and digital subtraction angiography.

Radiologists, radiographers, physicists and technicians alike will find *Assurance of Quality in the Diagnostic X-Ray Department* both a practical handbook for day-to-day use and a stimulus in developing their understanding of the scope of quality assurance.

November 1988 108 pages 296x208mm Spiralbound
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OPTIMIZATION OF IMAGE QUALITY AND PATIENT EXPOSURE IN DIAGNOSTIC RADIOLOGY

(BIR Report 20)

Editors:

B M Moores, B F Wall, H Eriskat and H Schibilla.

Contents: Introduction. Image Perception. Physical Assessment of Image Quality. Clinical Assessment of Image Quality. Optimization of Image Quality and Patient Dose - Paediatric Radiology - Mammography - Chest Radiography - Technical Factors. Patient Dose Measurements and Quality Assurance. CEC Image Quality and Exposure Criteria Trial. Panel Discussions. Conclusions and Perspectives for Future Research. CEC Study Group Document on Quality Criteria for Diagnostic Radiographic Images.

Key components in quality assurance in diagnostic radiology are image quality and patient exposure. Quality criteria defining optimum procedures should ensure that the most accurate and reproducible diagnostic information is obtained from radiographs, but at the same time minimize exposure of the patient to ionizing radiation. Formulation of such criteria was the aim of a workshop organized jointly by the CEC and NRPB, of which this book is the edited proceedings. A revised list of quality criteria for common diagnostic examinations was drawn up by a CEC Study Group and is appended to the proceedings.

October 1989   200 pages approx   266 x 196 mm
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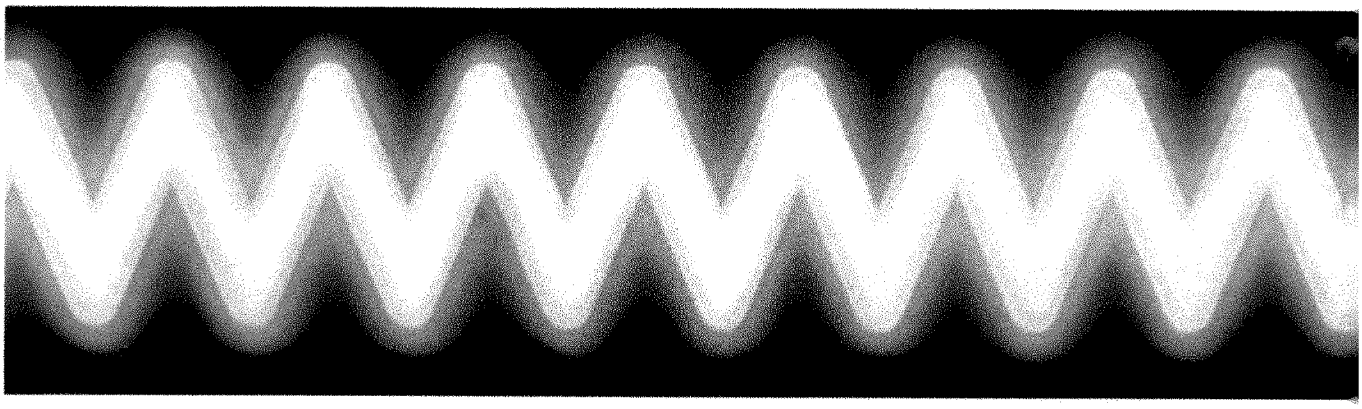

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The Scientific Basis of Modern Radiotherapy

(BIR Report 19)

Editor

N J McNally, Gray Laboratory, Mount Vernon Hospital, Middlesex

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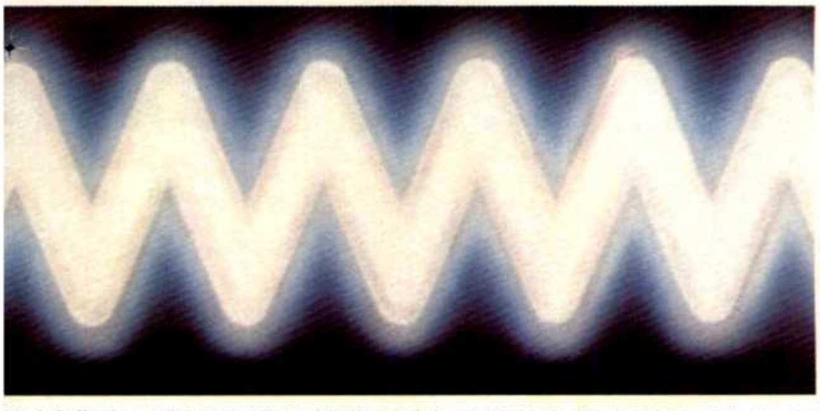

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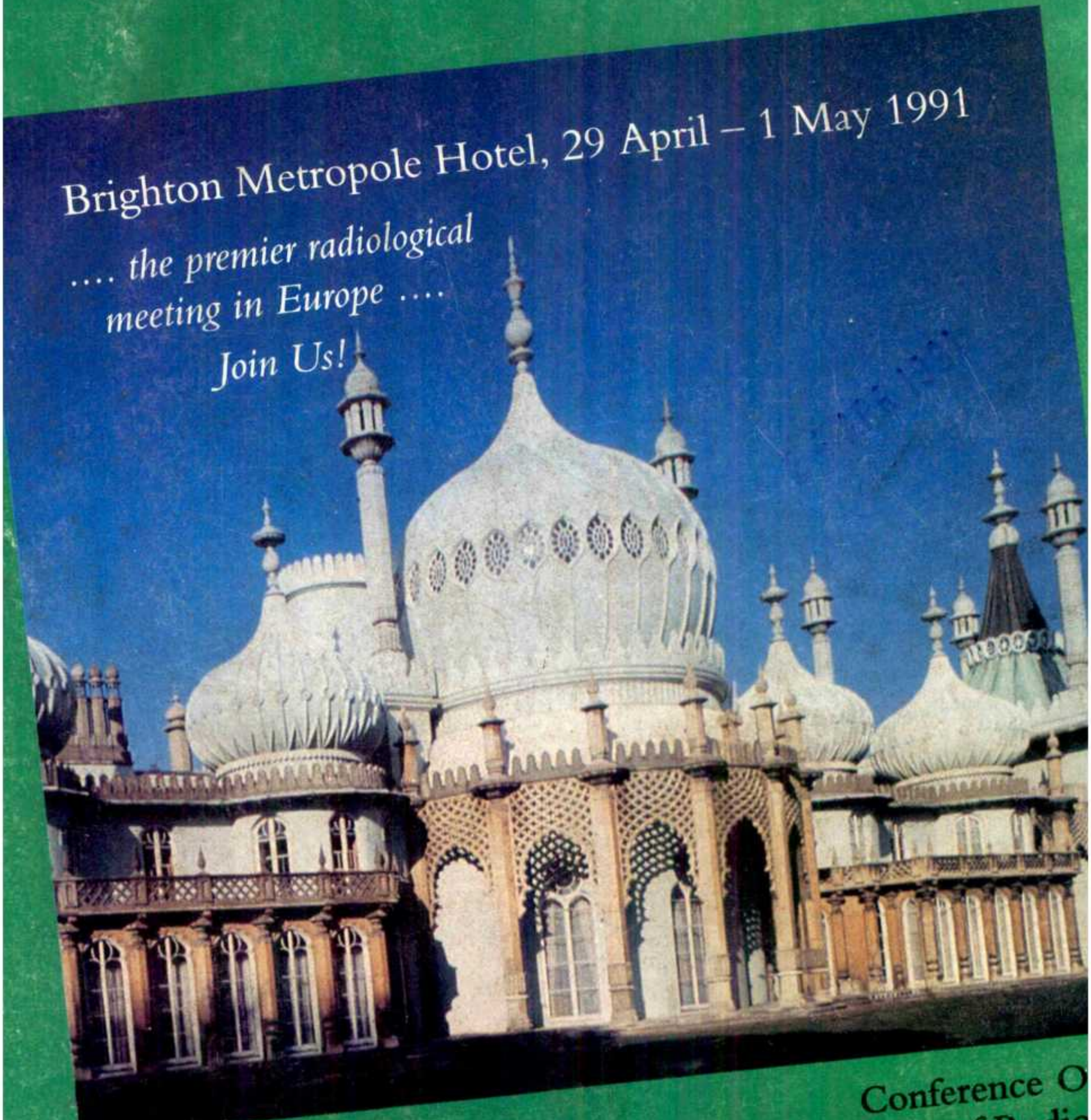

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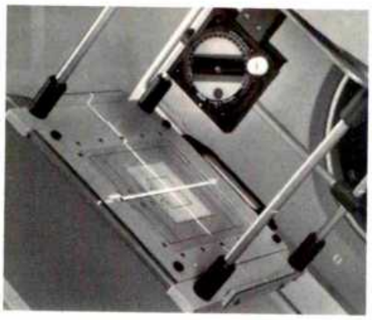

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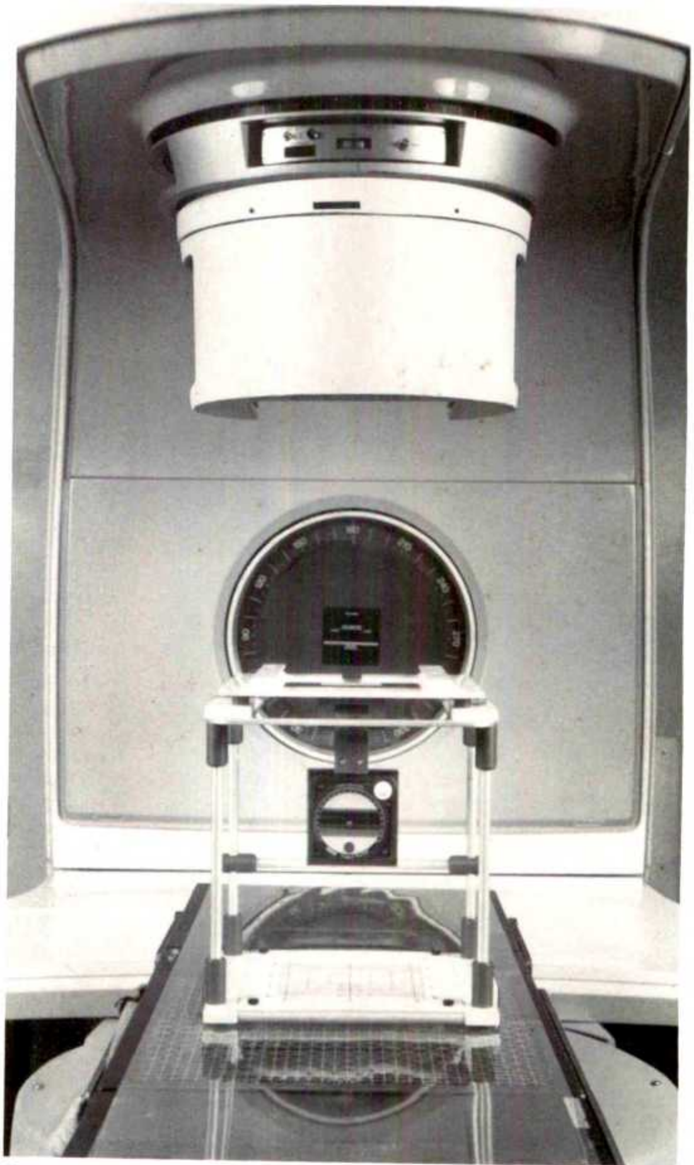

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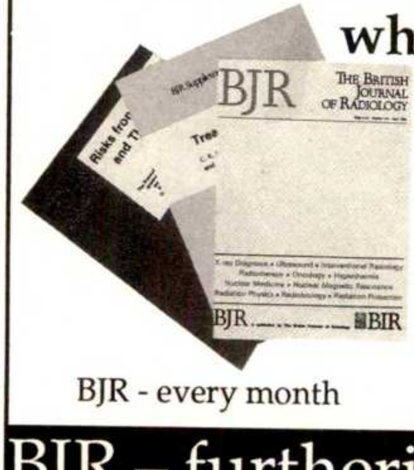

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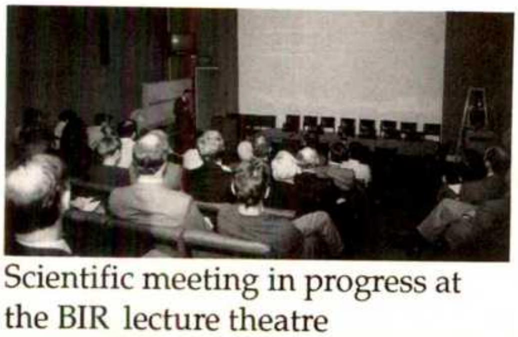

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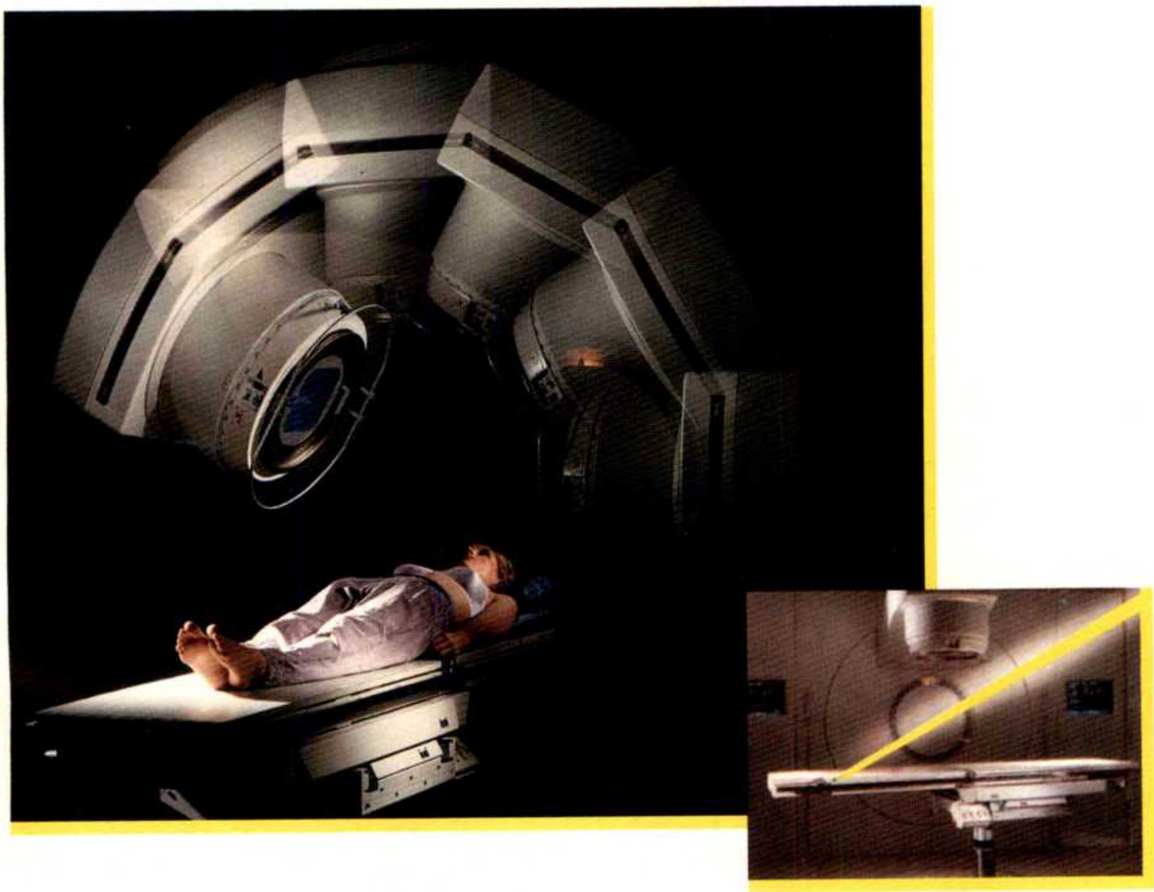

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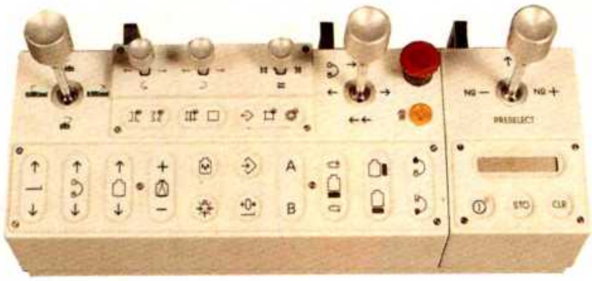

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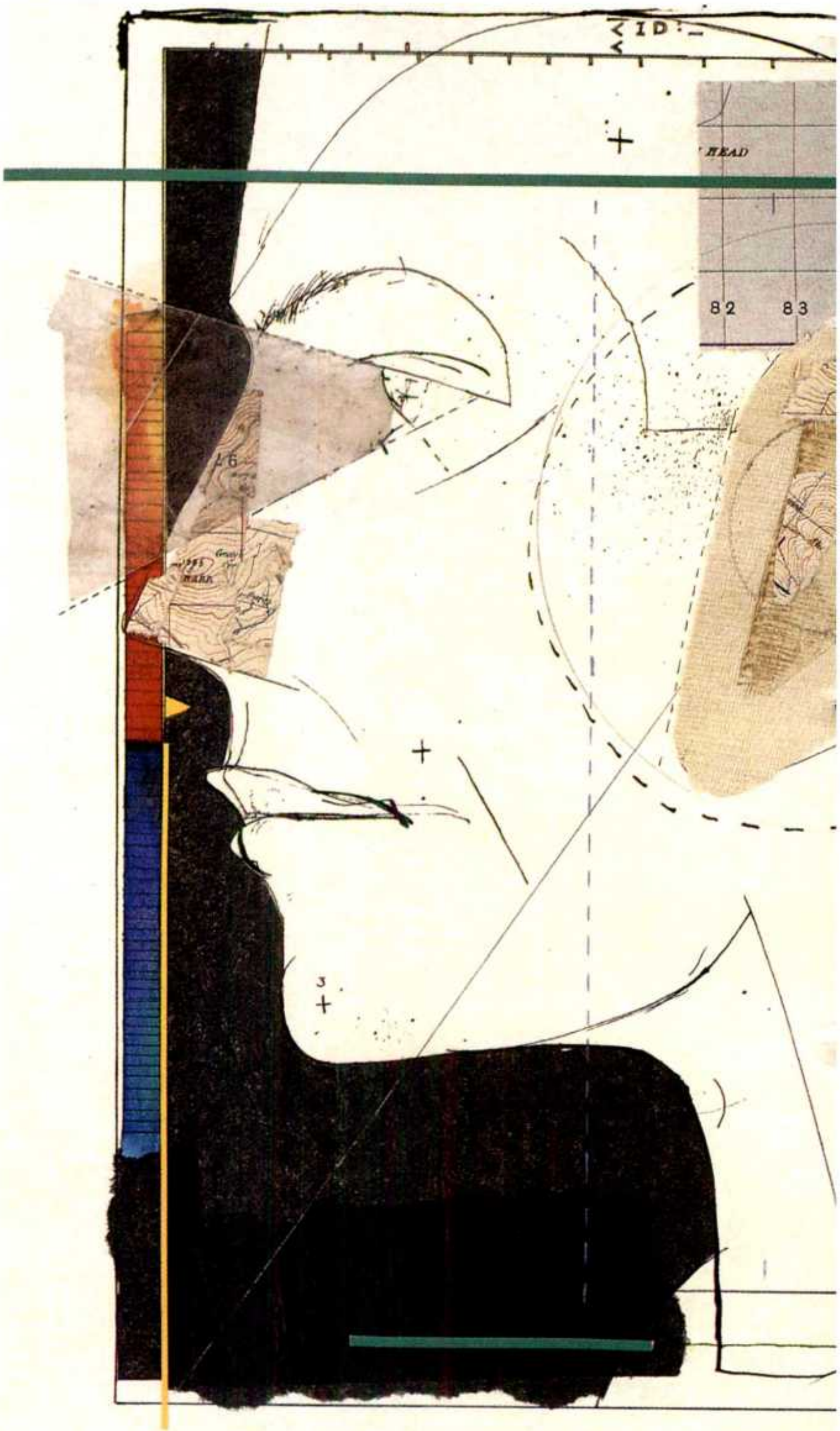

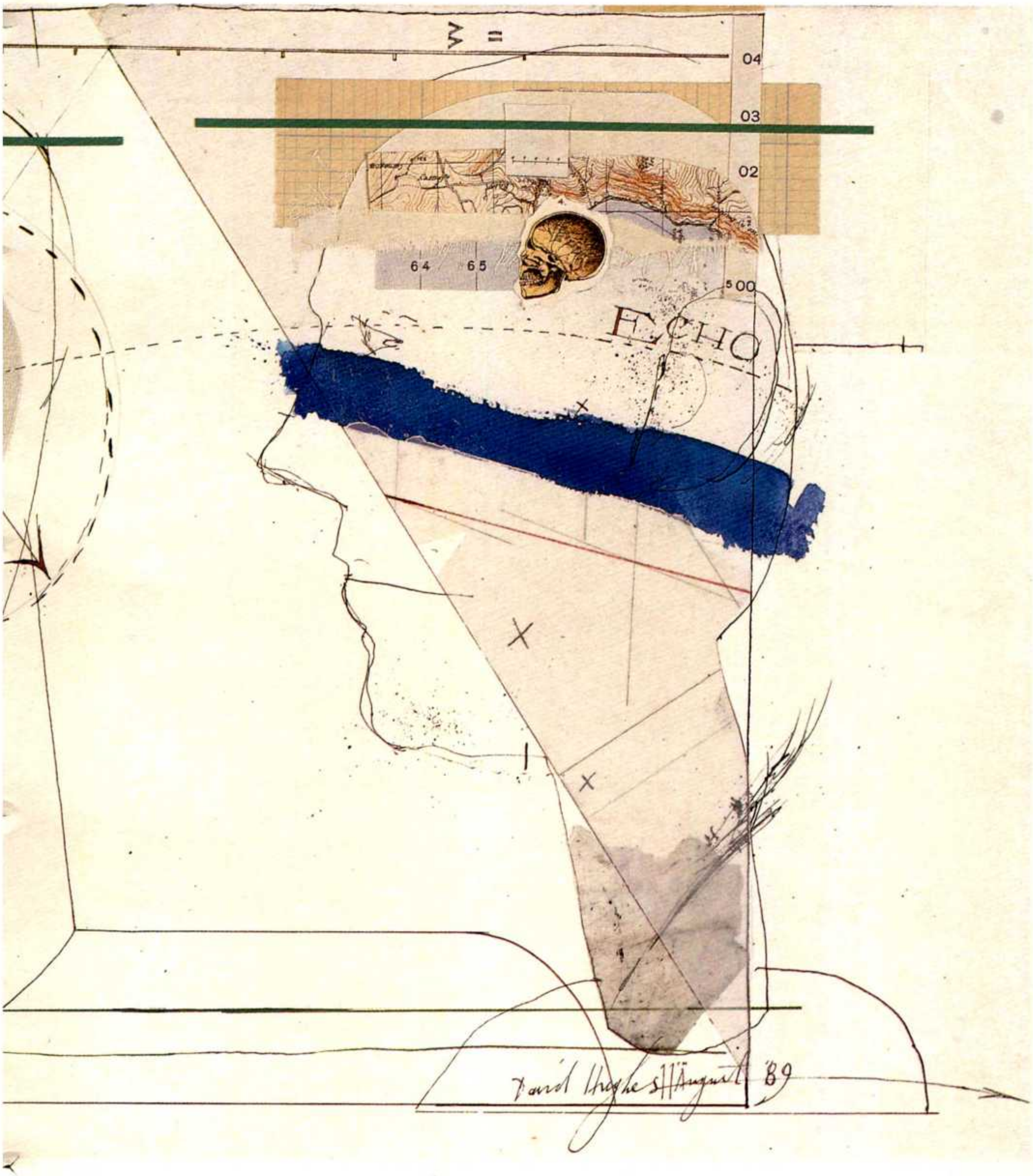

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The British Journal of Radiology

A future for radiological science?

British Institute of Radiology Presidential Address, 1990*

By C. R. Hill, DSc, FInstP, FIEE, HonFRCR

Physics Department, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey SM2 5PT

(*Received November 1990*)

Keywords: Radiology, Radiotherapy, Radiodiagnostics, Medical physics, X-ray, Computed tomography, Nuclear medicine, PET, MRI, MRS, Ultrasound imaging, Ultrasonic Surgery

The historical origin and continuing central raison d'être of the British Institute of Radiology is as an interdisciplinary forum for promoting the advance of radiological science. This preculiar, broad, generalist but scientifically inclined concept of an institution is one that many of us who are part of it cherish very warmly. I certainly share this feeling, but I also believe that it behoves us from time to time to stand back and examine, from a wider perspective, what we are aiming to achieve, how we fit in to the contemporary cultural environment, and which way the scientific frontiers of our subject are likely to move in the foreseeable future.

An objective outsider even from no further away than somewhere like Calais might well wonder whether the BIR was not in the same class as driving on the left side of the road: one of those quaint, if endearing, British institutions in which, in our insularity, we persist because we have not noticed that the rest of the world has passed us by. Surely, like it or not, we now live in an age of specialists, where the frontiers of physics have receded beyond the comprehension of many radiologists, while physicists, correspondingly, are equally out of their depth in many aspects of modern medicine.

Specialization is affecting us not only at the scientific level but also in the form of professional differentiation. In 1897, when the Röntgen Society was formed, its members were conscious of being either doctors or scientists: beyond that, they were largely content to be generalists. But the ethos of the late 20th Century has been towards technical differentiation and a corresponding tribalism built around the apparently secure havens of specialized professional bodies. This has been happening to all of us over the past 15 years or so, in radiology and radiography just as much as in physics and engineering, for reasons that are perfectly proper and are perhaps all the more understandable in the light of the indiscriminate public disenchantment with the scientific culture.

The damaging effect of this disenchantment on our own branch of science seems particularly ironic when we consider what must unquestionably be the enormous contribution to human wellbeing that has arisen during this century from our own, numerically rather small, branch of the applied physical sciences. It seems however to be, at least for the time being, one of the inevitable facts of contemporary life, and one that has found political and practical expression in the way that health care is financed and managed, not only in this country but also more generally. In many respects nowadays we find ourselves in a working environment where intellectual investment is allowable only if its returns can be guaranteed to be tangible and prompt—and preferably to occur within the current financial year.

Thus, for a number of inter-related reasons, the BIR, together with the objectives that it stands for, finds itself in a difficult if not even hostile environment. It therefore seems particularly important that we should take stock of the state of our principal assets, the hitherto unexplored regions of radiological science; for if those should dry up we really are in trouble, and we would be foolish to ignore such a possibility.

In what follows, therefore, I want to attempt a forward look at the scientific basis of our subject. Being myself a physicist, and with the belief that physics lies very much at the centre of the particular field of radiological science, I shall concentrate on physical aspects of the situation.

In a recent article Kenny (1990) very effectively questioned whether there is a finite limit to the progress of physics. There are good reasons for believing that this may be the case quite generally and, for the present, I would at least put the proposition that there will be real practical constraints, imposed by natural phenomena, that will determine certain limits beyond which an applied science such as ours cannot expect to progress.

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*Delivered at the BIR 1990 Annual Congress, Harrogate, June 1990.

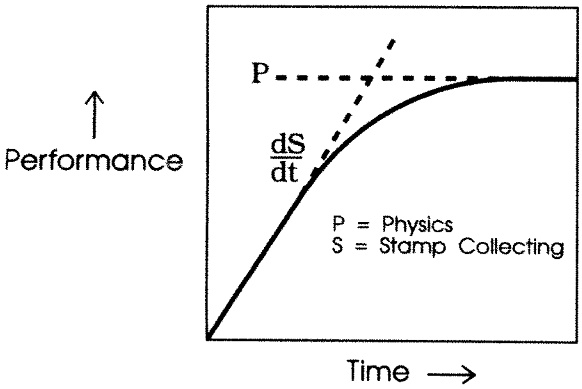

Figure 1. Anticipated time-dependence of general measures of performance in an applied science. Initially progress is rate-limited by the processes entailed in acquisition of knowledge and expertise: "stamp collecting" (S). Eventually however all measures of performance will approach an upper limit set by the fundamental physics (P) of the situation. It seems likely that the various branches of radiological science conform to this model.

Moreover, some aspects of current practice in radiology are already closely approaching such limits.

To have a framework for discussion of this situation it is useful to recall Rutherford's dictum that there are only two kinds of science: physics and stamp collecting. This has a degree of self-evident truth about it and also enables one to construct a useful mathematical model for the processes behind development of applied sciences in general, and radiological science in particular. Graphically, the predictions of this model are indicated in Fig. 1: performance in a given field of applied science, such as radiology, may be expected to advance steadily through the process of acquisition of relevant knowledge and expertise ("stamp collecting"), but only within an upper limit set by the fundamental physics of the situation.

Radiological science has bearing on both diagnostic and therapeutic questions. Let us look first at the diagnostic side. The past 30 years has been a tremendously exciting period in which to have worked in this field. In 1960 the only substantial and respectable medical imaging technique was the plain radiograph. Since then however both nuclear medicine and ultrasound have become mature and recognized, as have both computed tomography (CT) and nuclear magnetic resonance (NMR), neither of which were in any sense practicable even until the 1970s. It will be instructive, before considering the state of their respective scientific backgrounds, to note the current and prospective positions of these various techniques, in terms simply of the number of patient examinations to which they are being applied (Table I).

Table I. Relative numbers of radiological imaging examinations performed in Europe 1988–1993

	1988 Actual (%)	1993 Predicted (%)
X-ray	79	77
Ultrasound	17	19
CT	2	2
MRI	1	1
Nuclear medicine	2	2

(Source: Frost and Sullivan report E1111 summarized in *Rad Magazine*, *15* (164) Jan 1989).

The plain radiograph

The plain radiograph has been with us for a long time. We believe we understand fairly fully the physics behind its formation, although new and interesting twists are still turning up. As with any imaging technique, diagnostic quality depends, in an interactive manner, on several factors, and particularly on spatial resolution or MTF, contrast discrimination, frame acquisition time, patient "dose" and cost.

In the plain radiograph, contrast discrimination is inherently limited (even given optimum X-ray energy) by tissues over- and underlying the structures of interest, and also by scatter, whose suppression is tradeable against increased patient dose. For a given magnification, spatial resolution is principally limited by the properties of the detector and, however much the silver halide film may owe to serendipity rather than to science, it is difficult to conceive of a dose-efficient and otherwise practicable improvement on film or film–screen combinations.

There are other ways however in which physics may offer new opportunities, and it has only quite recently been appreciated that there is information potentially present (although perhaps at an excessive cost in patient dose) in the particular patterns of forward scattering that can be characteristic of molecular structure as such, rather than the atomic composition with which radio-

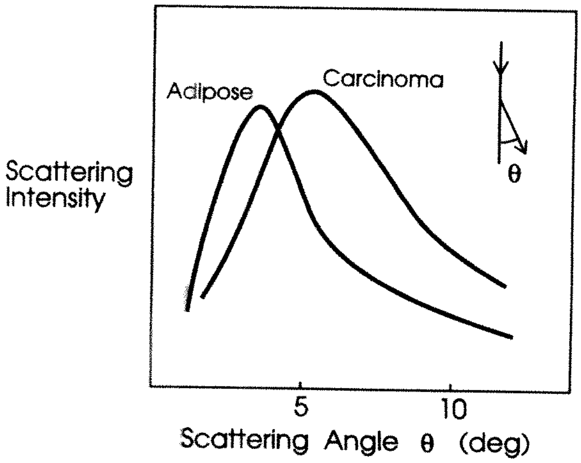

Figure 2. Angular distributions for the scattering of 46 keV (mean) X-ray photons in excised adipose and carcinomatous human breast tissue. Data of Evans et al (1991).

graphic X-ray interactions are normally associated. This behaviour is illustrated in Fig. 2 and is a consequence of the phenomenon of X-ray diffraction, which is familiar in its application to crystallography.

A very different direction in which there may be useful potential for further scientific exploration of the diagnostic X-ray process (as indeed for other medical imaging procedures) is in the psychophysics and ergonomics of optimally matching image information to the eye and brain of the radiologist, the central subject of the 1989 Presidential Address (Worthington, 1991). A particular problem here may arise with the introduction of mass mammographic screening which, in the UK alone, is expected to require the reporting of 3 million additional mammograms annually (Forrest, 1986). Physicists would contemplate the use here of computer-based pattern recognition techniques, and a recent study by Davies et al (1989) has shown that such techniques can match the ability of an experienced radiologist in detecting calcification clusters. Extending this approach to detect the more subtle mammographic signs of pathology will be a major but possibly achievable and certainly challenging task, whose successful outcome could have considerable implications for the cost-effectiveness of the procedure.

X-ray CT

The invention of CT came as a considerable embarrassment to most members of the medical physics community since, with hindsight, the principle and possibilities should have been "obvious" to us all. This is a lesson, therefore, that certainly gives pause for thought in attempts to pronounce on the future of the subject. Even bearing this in mind however, as also the comparatively short period of time that has been available for development of the subject, considerations of acceptable patient dose and theoretically achievable detector sensitivity for a given spatial resolution all seem to point to the conclusion that current performance is approaching the "physically determined" limit on the S–P curve of Fig. 1.

It will be observed here however that the P-level considered in this context is not set purely by considerations of physics, but has folded into it judgements on acceptable radiation hazard, thus bringing in considerations not only from another branch of physics—radiobiology—but also, more imponderably, elements of psychology and even politics. Even so, future prospects for resolving uncertainties of this kind would seem unlikely to result in any substantial long-term increase in the relevant P-level.

Nuclear medicine

The ability, by means of radiolabelled pharmaceuticals, to investigate the metabolic characteristics of disease on an anatomically related basis seemed to be an enormously attractive prospect in the 1950s and 1960s. It therefore seems remarkable that, in 1990, nuclear medicine has only a rather limited role within the radiological community.

There may be several reasons for this. In the first place, most modern physicists and even many radiologists (unlike W. S. Gilbert's Modern Major General) do not have the background to feel entirely comfortable in matters biochemical. More important however for this discussion may be the currently achievable quality of nuclear medicine images, which are greatly inferior to most other radiological experience on all three counts of spatial resolution, contrast discrimination and acquisition speed. However, current practice still seems to be greatly below the P-level. This subject was discussed much better than I could in a recent BIR Mayneord Lecture (Ott, 1989) and I shall only try to summarize the situation.

The instrumental basis of modern, conventional nuclear medicine is the so-called Anger Gamma Camera. Viewed objectively however by radiation detector physicists, this device appears to be a technological dinosaur. In order to achieve reasonable directivity the detector crystal is screened from the patient by a massive slab of lead, pierced by small holes: the "collimator". The immediate effect of this is a drop of photon efficiency by a factor of between 1000 and 10 000. This in turn degrades achievable spatial resolution, while scatter from the collimator leads to image noise and thus poor contrast discrimination.

It seems surprising therefore not only that a physically much more satisfactory design of instrument is possible, but that it was actually conceived more than 30 years ago and has now been available for some time in commercial form. I refer of course to the positron camera. The positron camera principle achieves directivity through the physics of the 180° photon-pair geometry, thus dispensing with the need for a collimator and leading to a photon efficiency that is limited only by detector design and can in practice approach 50%. Spatial and contrast resolution can be correspondingly good.

How then has nuclear medicine missed out on this possibility? I would suggest that this has more to do with perceptions and fashion than it has with science and engineering, or even with scientifically informed economics.

Positron emission tomography (PET) was conceived as a method of coping with the natural property of isotopes of the light elements to be incapable of emitting γ rays but to be happy to provide positrons. The traditional hardware that has evolved is inherently very expensive and, moreover, the usable isotopes of oxygen, carbon and nitrogen that are of particular interest all have half-lives measured in minutes, so that the cyclotron that produces them must be on-site and essentially dedicated, all of which makes for a multi-million pound installation. From here on, however, logic has broken down and the false perception has arisen that, because the PET principle lends itself to high level studies of the human metabolism of compounds containing oxygen, carbon and nitrogen, it is not an appropriate tool in nuclear medicine.

It is well known, however, among high energy physi-

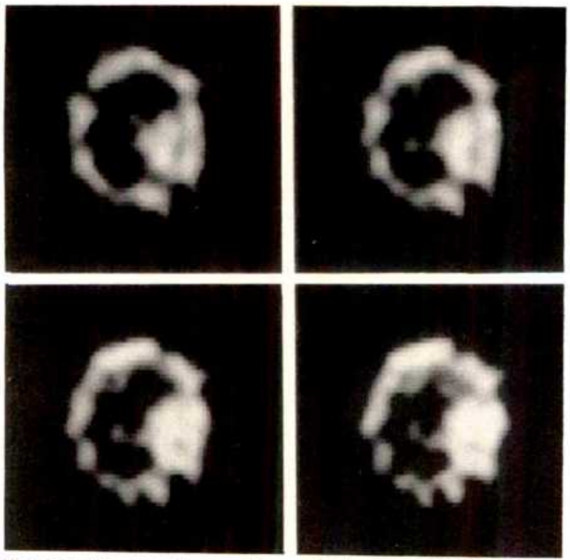

Figure 3. Four contiguous, 6 mm thick, transaxial PET images through the brain of a patient with a large, vascular glioma. The scans show a high uptake of ^{68}Ga-EDTA in the region of blood-brain barrier damage. Scans obtained on a prototype, multiwire proportional chamber PET camera, "MUPPET", with radiopharmaceutical derived from an in-house ion exchange generator (Ott, 1989).

cists, that spatially resolving, large area detectors can be made quite economically. With a pair of these, one can make a perfectly good positron camera: Drs Ott and McCready have had one such built and in clinical use at The Royal Marsden Hospital for the past 3 years (Ott, 1989). Moreover, the actual range and properties of positron-emitting radioisotopes are such that, by the use of ion-exchange generators where necessary, it is probably possible to produce a range of radiopharmaceuticals at least as comprehensive as those currently in use for single-photon nuclear medicine, without the need for dedicated, on-site cyclotrons. An example of an early clinical application of such technology is shown in Fig. 3.

Hitherto, nuclear medicine has been regarded by most radiologists as being outside their province, and perhaps this will remain the case. They should be aware however that here is an area of radiological science, in its broadest sense, that may well be poised for a "great leap forward" and one that would give us the tool that would not only achieve quite respectable imaging performance but, more importantly, relate this to very sophisticated and clinically relevant information about normal and pathological patterns of metabolism. Thus, both for aspiring scientists and thoughtful radiologists, this should be an area of the subject worth watching with interest.

NMR

For a physicist trying to make prophetic utterances about the future of radiological science, the advent of nuclear magnetic resonance imaging (MRI), like that of CT, is a sobering object lesson. Which of us, if asked 20 years ago to identify a physical principle around which one might construct an effective medical imaging technique, would have suggested NMR? Not many! And yet, a few years ago, it was authoritatively suggested that NMR might indeed constitute the "ultimate imaging window". Most physicists nowadays would probably have to agree, but one sometimes wonders why we should be so sure when we have been caught out so badly twice in the past 20 years!

In a sense, the remarkable thing about MRI is that it works at all. In principle it entails inducing a shock disturbance in the statistical equilibrium of nuclear spins within a tissue volume and then listening for the next second or so to the radiofrequency signals corresponding to the return to equilibrium. But these signals have to be extracted from a very large set of random signals, or noise, corresponding to the natural random movements of the spins. It is this signal and noise relationship that sets the fundamental limit to both imaging and spectroscopic performance: a limit at which current technique has already effectively arrived. In this sense we appear already to have reached the P-level of the phenomenon although we are, of course, at a fairly early stage in the "stamp collecting" process.

Fortunately however a number of trade-offs are possible. For example, deliberate limitation to a small volume of tissue, by use of surface coils, reduces the total noise level and thus enables improved spatial and contrast resolution. Similarly, within the limits imposed by radiofrequency penetration depth and tissue heating, signal-to-noise ratio can be improved by using higher magnetic field strengths, and this will be important in achieving good rapid acquisition performance.

Thus in MRI there will remain, for some time to come, some interesting challenges for physicists and engineers, with corresponding benefits for radiologists and their patients. We may nonetheless be coming in sight of the sort of plateau that has already been reached in CT.

Human magnetic resonance spectroscopy (MRS) is clearly at a much earlier stage of development than MRI and it is only in the last year or so, for example, that methods have been developed to do properly such basic things as localizing the source of tissue signals (Sharp & Leach, 1989) and quantifying the amounts of the various spectroscopic components that are recorded (Webb et al, 1990). Here again, however, even for phosphorous spectroscopy, which is one of the most favourable situations, the fundamental signal-to-noise problem is such that spatial specificity is unlikely ever to be better than a few cubic centimetres, even with the longest clinically tolerable acquisition times. This is of course biologically a very heterogeneous volume even when one is trying to focus on a nominally single entity, such as a tumour.

Magnetic resonance spectroscopy must still have plenty of mileage for physicists but, eventually, probably much more for biochemists. In practical application it is hard to see it becoming more than a very peripheral part of radiology, but its research potential is exciting and pharmacologists, for example, are already seriously considering the design of new drugs specifically to incorporate fluorine, so that their metabolism may be clinically assessed using both PET and NMR.

Ultrasound

Ultrasound presents us with an enigma. Its use is growing rapidly: in one major London Health Authority, for example, it accounted for some 20% of all imaging examinations in 1989 and that percentage had been growing steadily by 6% per year over the previous 6 years (Dr W.R. Lees, Personal communication). And yet, at least in the sense that clinicians often find them unintelligible, it is clear that the quality of contemporary ultrasound images generally leaves much to be desired. A few months ago a young senior house officer retailed his colleagues' definition of ultrasound as "what you get when you unplug the TV aerial".

Why then is image quality so bad? What indeed is the fundamental and detailed process of formation of ultrasonic images that is responsible for this? One would expect physicists to know, but the embarrassing thing is that we do not, or certainly not at the level of detail at which we can explain the processes of formation of X-ray, radioisotope and even NMR images.

We are of course learning. It is a central tenet of image science that image noise is all-important in determining interpretability. Ten years ago there was little systematic knowledge about the dominant source of noise in ultrasonic images but we now know that this is coherent radiation speckle and we are starting to find systematic approaches to mitigating its ill-effect on the diagnostic process (Bamber & Daft, 1986; Bamber & Cook-Martin, 1987; Hill et al, 1991).

At a different level our understanding, and therefore optimum use, of the conventional pulse-echo imaging principle is limited because we have not yet discovered the detailed acoustic histology of tissues, although we do already know that this differs considerably as between different tissue types.

There is also an extra dimension in which ultrasound differs from the phenomena behind the other imaging techniques that I have previously discussed. In terms of physics, pulse-echo imaging is an attempt to display a map of a particular physical quantity that is locally characteristic of a tissue: its backscattering cross-section. However, unlike the situation with X-rays (although with some admitted analogy with MRI) ultrasound offers a number of other and essentially independent physical properties of tissue that have been shown to be exploitable for imaging, each exhibiting its own very different contrast mechanism (Hill et al, 1990). Attenuation coefficient and sound speed are just two examples, and others have been illustrated in this year's Mayneord Lecture by Dr Lizzi (1990). As one further example I would remind you that a class of contrast mechanism to which ultrasound is particularly well adapted is tissue movement, whether this be as a fluid flow or the deformation behaviour of soft tissues. We have already seen useful outcome of this in the form of Doppler colour flow mapping, but much more is yet to come (Tristam et al, 1986, 1988; Lerner et al, 1990).

Thus I would argue not only that the scientific basis on which ultrasonic imaging is at present conducted is (as for nuclear medicine) still some considerable way below its P-level, but also that, uniquely for a current medical imaging phenomenon, we do not yet know quite how far ahead its P-level may eventually prove to be.

Meanwhile, stamp-collecting goes on apace. During the 1970s for example, there was a general impression that difficulty of acoustic access to many parts of the body was bad news for ultrasound. However, with the increasingly adventurous willingness of radiologists (and also, notably in recent years, surgeons) to insert trasducers into all conceivable body orifices, there seem to remain few no-go areas other than the inflated lungs and adult brain (Holm, 1990).

In summary, therefore, with the prospect of a combination of substantial further physical discovery, together with engineering and medical inventiveness, the ultrasonic branch of radiological science seems to have a healthy future.

Radiotherapy

Any interested onlooker of the radiotherapy scene over the past 30 years must have sensed, at least following the successful introduction of cobalt and linear accelerators for deeply penetrating beam therapy, a degree of inertia in the progress of the scientific basis of the subject. This has not been for lack of interesting ideas and we have seen successive attempts to exploit such apparently promising agents as hyperbaric oxygen, fast neutrons, boron capture of thermal neutrons, ion beams, hyperthermia and hypoxic cell sensitizers, but all with rather limited and controversial success.

The essential aim in radiotherapy is to achieve a good positive balance between malignant tissue destruction and preservation of normal function. For physical science and engineering this seems to pose two complementary groups of problems: first, to locate precisely and reliably the geometrical limits of proliferating neoplastic tissue and, secondly, to generate radiation dose distributions that conform well to those limits. Clearly, advances in one of these areas are of little use without the other and it is therefore remarkable that, as early as the mid-1960s, considerable financial and intellectual investment was being made to develop beams of heavy ions and negative pi-mesons that would localize very tightly within millimetre dimensions.

Since then, tomographic imaging techniques have been developing out of all recognition and, if they can achieve the reliability and sensitivity unambiguously to identify tumour deposits, it may become worth reconsidering the more general use of these sophisticated radiation beams for highly precise localization of therapy dose. As it is, however, the impact of computer technology, both on linear accelerator beam control and on

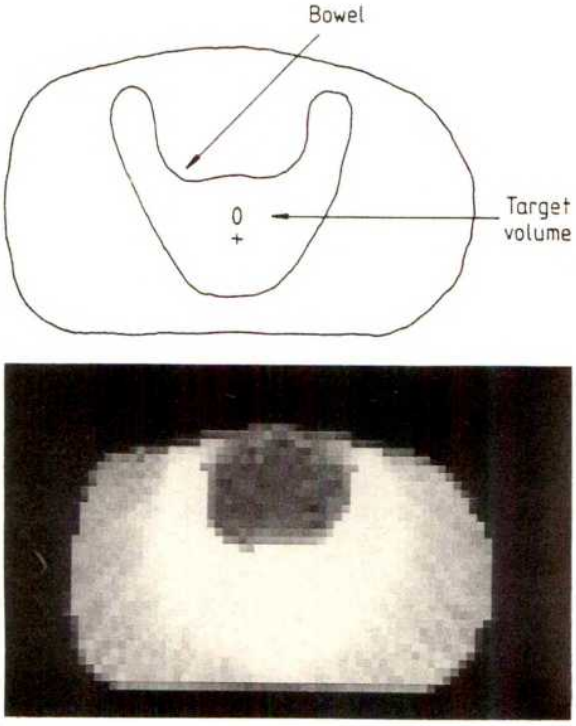

Figure 4. A solution to "Lee Chin's Planning Problem" developed for use on a computer-controlled linear accelerator. The diagram illustrates a target volume comprising a rectal lesion and inguinal nodes, where it is required to spare as much of the bowel as possible. Shown below is a computed solution to the problem that uses multiple beams and a "simulated annealing" procedure for optimizing dose distribution (Webb, 1989). (Reproduced, by permission, from *Physics in Medicine and Biology*.)

three-dimensional treatment planning, is breathing new strength into the use of more conventional beams. Some aspects of this development are illustrated in Fig. 4.

Thus imaging, and particularly the CT scanner, has gone a long way to provide a satisfactory basis for effective planning, but the problem of sensitive tumour identification remains. Now it is arguable, if we can make effective use of undoubted metabolic differentials, that the best hope here may be PET and it is possible that we may soon therefore see the advent, partly for radiotherapy planning purposes, of hybrid X-ray CT/PET scanners when, perhaps, metabolic data will appear colour coded and directly superimposed on a conventional CT image.

A major remaining problem in radiotherapy is to achieve sufficiently prompt assessment of therapeutic response of a particular tumour so that the therapy can be appropriately adjusted. Here surely is an area of radiological science, in its broadest sense, that has real prospects for an interactive combination of fundamental advance in understanding and substantial practical outcome. Conventional radiobiology is already moving well towards providing specific assays of the therapeutic response to individual human tumours, and showing objective laboratory evidence for a considerable variability in such responsiveness. As the emerging methods of molecular biology can be brought into practical application here we should start to see the beginnings of a cybernetically respectable strategy for intelligent control of therapeutic management, on the basis of continuous information feedback (Wiener, 1961).

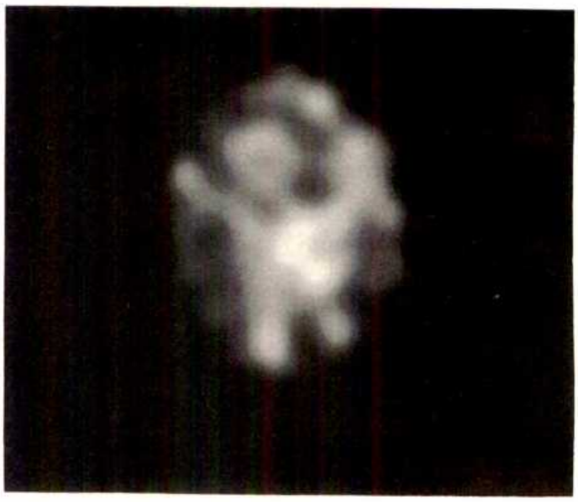

Figure 5. A 6 mm slice-thickness transaxial MUPPET image (as for Fig. 3) showing the distribution of ^{18}F-FUDR in normal brain tissue and glioma. The enhanced uptake in tumour is indicative of rapid cell proliferation. (Illustrations for this and Fig. 3 kindly provided by Dr R. J. Ott.)

Imaging techniques should have an interesting role here too. Even at the purely anatomical level it is far from clear at present that the planning geometry remains precisely reproduced throughout a course of treatment, when both the tumour and normal anatomy may become substantially modified. We may need to learn quite a bit about this, and correspondingly expect to modify routine practice, with the use of imaging techniques, both plain and tomographic, that are integral with the treatment machines.

Another more speculative but potentially exciting role for imaging in radiotherapy is in relation to the biologically based assessments of therapeutic response, referred to above. With the practical introduction of affordable PET as an arm of routine nuclear medicine, one may expect development of methods for assaying changes in tumour- and normal-cell proliferation rates, by the use of radiolabelled pyrimidines (Fig. 5). At the same time, at least in research settings, it will be possible to derive complementary information on changes in cell turnover rate as evidenced by localized NMR phosphorus spectroscopy measurments of phospholipid metabolism (Glaholm et al, 1989).

Thus, in summary, the received wisdom in radiotherapy may have been too influenced, perhaps unconsciously, by the perception that its technical basis had about reached a basic limit imposed by physics. It now seems that this may have been a misconception due to taking too narrow an interpretation of the scope of physics—which in truth embraces radiobiology, tumour physiology (as lucidly described by Denekamp (1990) in her Sylvanus Thompson lecture), molecular biology, and even aspects of biochemistry. These, together with improved correspondence between tumour anatomy and dose distributions, may be the areas of our subject in which to look for substantial progress in the next few years.

Radiative approaches to tumour ablation

It is worth recalling that, historically, conventional radiotherapy was born of pure empiricism. Röntgen's and Curie's discoveries had seized the professional and public imaginations and seemed to offer an undreamed of opportunity for local tissue destruction in situations where surgery was impracticable. Indeed, it was largely the surgeons who pioneered the art of radiotherapy in its early days.

As we now know, even as an approach to local tumour control, radiotherapy has its limitations: some tumour types, or even sub-populations, are radioresistant; some tumours seem to harbour radioresistant environments, and the goal of destroying the proliferative ability of 100% of even a radiosensitive tumour cell population is often impossible to achieve.

In this situation we may need to do some lateral thinking and consider what we are trying to achieve and, given what we now know about radiation science in its broadest sense, whether there may not be other and complementary technical approaches to our objectives. Indeed, lateral thinking or no, we are aware that other radiation based approaches to localized tissue ablation are already being tried and it is again the surgeons who are leading the way.

A well known example of this development is laser surgery, used either on its own for thermally mediated tissue destruction or, as so-called photo-dynamic therapy (PDT), through the interaction with a medically administered photo-active substance: so-called "haematoporphyrin derivative". This is a field that poses some interesting questions in its underlying physics and chemistry. Indeed, it is interesting that one of the claims for PDT is that it exploits a degree of tumour specificity that is said to be exhibited by porphyrins (Jori & Spikes, 1984), and yet there seems to be little or no evidence for such behaviour from the very considerable work, in nuclear medicine and elsewhere, that has been put into searching for the philosopher's stone of a generally tumour specific substance.

Closer perhaps than laser light to having a home in mainstream radiological science is ultrasound. This was shown, at least as early as the 1950s, to have potential for deep and highly localized tissue ablation (Wall et al, 1953).

Remarkably, in view of the need to raise a skull flap in order to gain acoustic access, its main area for clinical trial was, for a considerable period, the brain. More recently, one or two other sites have started to attract interest, one example of which is the orbit, referred to by Lizzi (1990) in his Mayneord Lecture. There seem to be no clear practical or scientific reasons why this possibility has not been followed up more actively in other anatomical sites: this may be yet another example of the way that subjective perceptions influence the progress of science more than we sometimes like to admit.

There is a set of interesting features of focused ultrasound which, when considered together, seem to make a strong case at least for serious scientific study of this

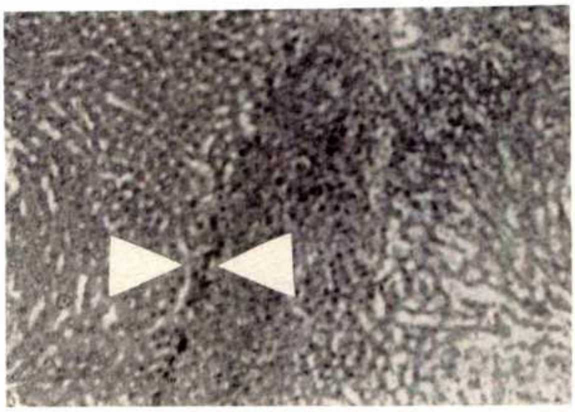

Figure 6. Histological section of rat liver showing the very narrow (ca. 6 cell diameters) boundary region (arrowed) achievable, using focused ultrasound lesioning, between regions of undamaged (upper left) and totally destroyed (lower right) tissues.

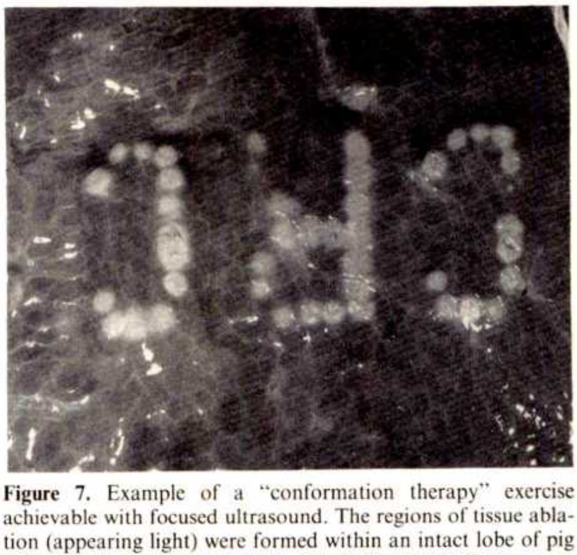

Figure 7. Example of a "conformation therapy" exercise achievable with focused ultrasound. The regions of tissue ablation (appearing light) were formed within an intact lobe of pig liver, at a depth of about 3 cm, without histologically apparent superficial damage. They are seen here following sectioning of the liver. (Research funded by Cancer Research Campaign (CRC) and illustrations for this and Fig. 6 provided by Gail ter Haar and Ian Rivens.)

phenomenon as a basis for local control of some tumours. First, and in a sense most importantly, there are good prospects that such beams will be able to achieve their ablative potential at a number of interesting tumour sites. This situation is now looking better than might at first have been anticipated with the increasing willingness of surgeons to carry out preparatory and, by their standards, relatively straightforward surgical procedures in order to open up an adequate acoustic access window: for example, to fold back ribs in order to enable treatment of solitary liver metastases.

Then, when access to the target region has been achieved, the lesion that can be produced is geometrically very clean: whilst complete sterilization of cells is achieved in the focal region, the boundary between that and entirely undamaged tissue is very sharp: only some 6 cell diameters in extent, as illustrated in Fig. 6.

Furthermore, the evidence from animal work is that if the tumour is entirely encompassed by the focal region it can be totally ablated, without subsequent local recurrence and, at least for liver tumours, without scar formation during its replacement with regenerated normal tissue.

Thirdly, an interesting feature of focal lesions formed in this way is that, for reasons that are still unclear, they are well visualized on ultrasound. This seems to provide a promising approach to monitoring the success of the treatment in covering the intended target.

Finally, as mentioned above, there is much interest among radiotherapy physicists in achieving precise geometrical conformity between dose delivery and the rather awkward shapes exhibited by some tumours. As illustrated in Fig. 7, this is a facility that is also well exhibited by focused ultrasound.

Conclusions

In summary, the answer to the question whether there is a future for radiological science must be "Yes indeed—but ...".

In his great book *Religion and the Rise of Capitalism*, R.H. Tawney discussed the breakdown of spiritual and social values that, as many believed, came with the widespread adoption of the practice of usury which, long before, had been characterized by Aristotle as "The most hated sort of wealth, and with the greatest reason, since it makes a gain out of money itself, and not from the natural object of it".

Tawney wrote at a time of great changes in social values and public perceptions. It seems that we may now be experiencing another period of change in these respects and perhaps there will soon be a place for a corresponding treatise: *Radiology and the Rise of Monetarism*. This is, in the true sense of the word, a political issue, but it is one that far transcends national or party politics. The past quarter century has seen, in Britain and North America particularly, and in addition to the apparent public disenchantment with science referred to earlier, a substantial and worrying shift towards financial short-termism. While this shift might have been at least understandable in commerce, its extension to central government policy has profound implications for many areas of science and education, including in particular those represented in our own Institute and, in the long run, for the quality of the society which these support.

This seems to be a matter of public perception, or perhaps misconception, as much as anything else and if we are to halt and reverse this trend it will be essential that, as Disraeli remarked in a similar context, "We must educate our masters".

Let us look on the bright side though, and assume that this can be achieved. What then?

I hope that I will already have made the point that, whatever it may be, the foreseeable future of radiological science will certainly not just be "more of the same". The examples that I have chosen naturally reflect my own interest, experience and enthusiasms and those of some of my close colleagues. I hope however that these examples are not totally unrepresentative. If this is so, two broad conclusions seem to follow. In the first place, those who are looking to make a research and academic career in our field will be wise to look thoughtfully before deciding to specialize in some of the more "obvious" branches of the subject. Or, seen more positively, there is still a good range of exciting new possibilities for research and development. Secondly, working radiologists and radiotherapists should be prepared for some surprising changes in the scientific understanding, and eventually the routine practice of their art.

Acknowledgments

I am indebted to a large number of my colleagues on whose work and ideas much of this paper is based, to the Cancer Research Campaign for grant support of much of that work, and to Prof. Ralph McCready and Dr Steve Webb for helpfully commenting on the original text.

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Quantitative computed tomography for bone mineral measurement: technical aspects, dosimetry, normal data and clinical applications

By A. H. Karantanas, MD, J. A. Kalef-Ezra, PhD and D. C. Glaros, PhD

Departments of Medical Physics and Radiology, Medical School, University of Ioannina, Ioannina 451 10, Greece

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Abstract. A single KV_p quantitative CT (QCT) technique was used for measuring the spinal trabecular bone density. The trabecular bone equivalent density (TBED) was expressed as the density of a K_2HPO_4 solution that exhibits a linear attenuation coefficient identical to that of trabecular bone. A field non-uniformity correcting factor was obtained from experiments on phantoms. The effective equivalent dose of the whole examination (four sections and a scout view) is 370 μSv. The *in vivo* short-term precision (reproducibility coefficient of variation) ranges from 1.4% to 4.1% depending on the TBED values of the normal subjects. The TBED was measured in 206 normal Greeks aged 30–69 years. Average TBED decreased with increasing age for both sexes. Analysis considering separately each vertebra showed a tendency to a caudal spinal TBED reduction. No correlation was found between the TBED values and the body habitus, milk consumption, smoking habits in men, and number of full-term pregnancies. A significant difference ($p < 0.01$) was found between the TBED values of the normals and those of 50 women suffering from post-menopausal osteoporosis, 37 alcoholic men, and 12 gastrectomized men (Billroth II). Quantitative CT has been established as a method of measuring TBED in health and disease, and the results from this study confirm these applications.

Osteoporosis is a major social and economic problem (Riggs & Melton, 1986; Rogers, 1987). This syndrome is characterized by increased vulnerability to fractures (Lukert, 1982; Lane & Vigorita, 1983; Melton & Riggs, 1987) that usually occur after a minor trauma. Vertebral fractures are thought to result predominantly from a loss of trabecular bone (Genant et al, 1982; Oravez & Robertson, 1987). Trabecular bone is assumed to be the most significant factor affecting the mechanical strength of the vertebral bodies (McBroom et al, 1985; Biggemann et al, 1989). The spinal trabecular bone, because of its high turnover rate, is the preferential site for early detection of bone mineral alterations (Snyder et al, 1977). Therefore, it is of clinical relevance to estimate the bone mineral density in the region of thoracolumbar spine (Melton et al, 1988).

Various methods have been developed to assess skeletal status quantitatively (Cohn, 1981; Wahner et al, 1984a, b; Glaros et al, 1987; Goodwin 1987; Melton et al, 1988). Quantitative computed tomography (QCT) of vertebral bodies can separate the trabecular bone from the cortical shell and the posterior elements. The value of QCT in studying mineral density of the spinal trabecular bone has been widely investigated technically (Genant & Boyd, 1977; Cann & Genant, 1980; Kalender et al, 1985; Reinus & Nadel, 1987; Rao et al, 1987) and applied clinically (Cann et al, 1980; Firooznia et al, 1986; Fujii et al, 1987; Montag et al, 1987; Compston et al, 1988; Karantanas, 1989).

In this study, data is presented on the following: (1) precision and accuracy of the technique, (2) dosimetry and risk factor, and (3) bone density of normal Greek adults and of patients whose clinical conditions are related to osteopenia.

Materials and methods

Technique

A single KV_p technique (Cann & Genant, 1980) was applied (125 KV_p, HVL: 0.6 mm Cu) with a commercial CT scanner (Siemens, Somatom DR2-G). Reference solutions of K_2HPO_4 with concentrations 0, 50, 100, 150 and 200 mg cm^{-3} in 2 mm thick Plexiglas tubes were used for calibration. The interaction properties of photons with K_2HPO_4 are similar to those with $Ca_5(PO_4)_3OH$, for the photon spectra used in CT (Hubbell, 1982).

The subjects lie in supine position with the upper limbs extended above the head. The hips are flexed to straighten lumbar lordosis and improve the contact with the reference solutions positioned under the subject's back. A lateral digital radiograph (256 mm in length), starting from the xiphoid level, was used to position the gantry for 8 mm thick axial scans, through the mid-portion of the vertebral bodies T_{12}, L_1, L_2, and L_3. The following programme was used for the axial scans: 125 KV_p, 60 mAs, 240° tube rotation. The scans were per-

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Address correspondence to J. Kalef-Ezra, PhD, Assistant Professor, Medical Physics Department, Medical School, University of Ioannina, Ioannina 451 10, Greece.

formed by the same technologist closely supervised by the same radiologist who performed all the measurements.

A region of interest (ROI), as large as possible, was drawn manually, excluding the posterior venous complex defect, areas of endosteal sclerosis and the cortical rim. The average CT number in every ROI was corrected for the deviation of the water value from zero (Brooks, 1977). The average CT number in the vertebral ROI was normalized, by linear regression analysis, against the CT numbers obtained from the reference solutions. The trabecular bone equivalent density (TBED) was expressed as the density of a K_2HPO_4 solution that exhibits an identical linear attenuation coefficient with that of the trabecular bone. A correction factor for field non-uniformity was determined and applied to the measurements.

Vertebrae with underlying apparent lesions, such as fractures, were excluded from the measurements. Measurements were not taken in cases where parts of the lung, colonic aeroplethia, contrast agents or excessive calcifications were included in the image.

The short-term precision was assessed by measuring twice 50 volunteers (TBED = 30–210 mg cm^{-3}) within a period of a few days and by repeated measurements in an elliptical human torso phantom. The intra-individual observer variation in the determination of the ROI in the L_1 vertebral bodies was determined in 20 subjects measured twice in 24 hours. The long-term stability of the system was assessed by estimating the CT numbers generated by the reference solutions over a 3-year period. Lithium fluoride thermoluminescent dosimeters (TLD-100) were used to determine the distribution of the absorbed dose in phantoms and patients and assess the corresponding radiological risk factor.

The following potential sources of systematic errors were investigated using a human torso phantom: size of the patient, cortical rim width of the vertebra as well as variation with location of the vertebra and the reference solutions in the field. The human torso phantom consisted of Plexiglas tubes of various thicknesses, filled with solutions of K_2HPO_4 and immersed in a water tank.

Subjects

Three hundred and five examinations were included in this study. One hundred and twenty-two normal women, aged 31–67 years (mean, 48 years) and 84 normal men, aged 30–69 years (mean 49 years) comprised the control group. The normal subjects were volunteers, who had no history of a clinical condition related to bone disease. Subjects under corticosteroid or heparin treatment and women on oral contraceptives were excluded. Lateral radiographs of the spine were required for subjects older than 45 years in order to investigate radiological signs of osteopenia (Gallagher et al, 1985; Reinbold et al, 1986; Ott et al, 1987). The following parameters were evaluated as potential factors affecting the TBED: body habitus, number of full-term pregnancies, milk consumption (greater or less than 400 ml of milk per day, or an equal quantity of milk products) and smoking habits in men (more than 20 cigarettes per day for more than 10 years).

Three groups of patients were included in the study.

The first group consisted of 50 women, aged 38–67 (mean 56 years) who were considered osteoporotic. They all were post-menopausal for at least 3 years (mean 10 years). These subjects were divided in four subgroups: (a) 13 presented with one spontaneous vertebral fracture and vertebral biconcavity, diagnosed on lateral radiograph of the spine, (b) five presented with abnormal Singh index and vertebral biconcavity, (c) nine presented with two or three spontaneous wedge vertebral fractures and (d) 23 presented with fractures at other parts of the skeleton which occurred after a minor trauma.

The second group consisted of 37 men, aged 30–68 years (mean 47 years) who were consuming more than 150 ml ethanol per day for at least 10 years. Five patients among them had hepatoma, and 18 had alcoholic cirrhosis, which was histologically verified. The remaining 14 patients presented total cerebral atrophy documented by computed tomography.

The third group consisted of 12 men, aged 35–63 years (mean, 50 years), who were gastrectomized at least 3 years earlier by the Billroth-II technique. Among them, only one reported a recent fracture consequent to a minor trauma.

Statistical analysis

The normal TBED data for men and women were analysed using linear, polynomial and exponential regression analysis. Tolerance intervals were determined. The difference of the variance was tested by *F*-test. The significance of differences between the various groups of subjects was tested by *t*-test.

Results

Technique

The dosimetric data on the technique showed that:

(a) the mean value of the absorbed dose in the midplane of each 8 mm thick slice is 2 mGy (Fig. 1);
(b) the computed tomographic dosimetric index (CTDI) is 5 mGy;
(c) the imparted energy of the examination is 9 mJ (3 mJ from the scout view and 6 mJ from the axial sections) and
(d) the effective equivalent dose of the examination is 370 μSv and the corresponding fatal risk factor is 5×10^{-6} according to ICRP (ICRP, 1977).

The short-term *in vivo* precision (standard deviation) was found to be 2.75 mg cm^{-3}, independent of the TBED value. The coefficient of variation ranges from 1.4% for young, healthy men of 30 years, to 4.1% for healthy, 65-year-old women. The short-term standard deviation for the 150 mg cm^{-3} K_2HPO_4 solution was found to be 1.9 mg cm^{-3}. It was found that an increase in radiation burden to the patient by a factor of eight

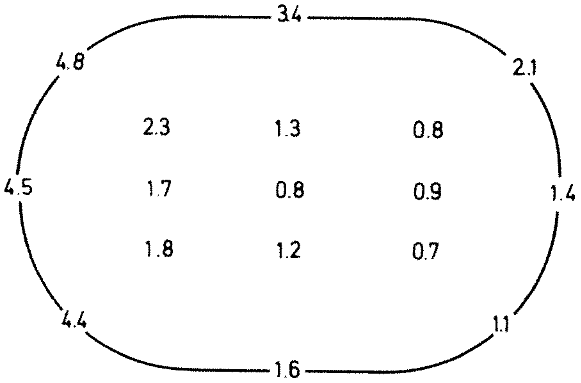

Figure 1. Absorbed dose distribution (in mGy) in the midplane of a 8 mm thick axial section in a homogeneous phantom of the human torso (240° tube rotation).

reduced the standard deviation to 1.5 mg cm^{-3}. The intra-individual observer variation in the determination of the ROI in the L_1 vertebral bodies was found to be 0.8 mg cm^{-3}. No systematic changes of the CT numbers were observed in the 3-year period, the standard deviation for the 150 mg cm^{-3} solution being 2.7 mg cm^{-3}.

The investigation on systematic errors showed that:

(a) the size of the human torso (range 40 cm × 15 cm, 40 cm × 18.5 cm, 40 cm × 22 cm) has minor influence ($< 2\%$) on the CT numbers of the reference solutions;
(b) the variation in positioning of the "vertebra" in the human "torso" does not influence the CT numbers of the vertebra;
(c) the width of the "cortical rim" of the "vertebra" does not influence the CT values of the ROI;
(d) the standard deviation of the CT values of water in the phantoms at distances more than 1 cm from the walls is 1.6 CT units;
(e) a statistically significant difference exists between the CT numbers in reference solutions depending on their position under the subject's back, therefore the reference solutions must always be positioned in the same order;
(f) the CT numbers of the water in the phantom are, on the average, four CT units lower than the water CT number in the reference solution;
(g) there is a linear relationship between the CT numbers and the K_2HPO_4 concentration as well as the electron volume density (Fig. 2), and
(h) the CT numbers of each K_2HPO_4 solution was significantly different ($p < 0.01$ in the trabecular bone phantom and in the tube under the subject's back. Therefore, the measured TBED values, $TBED_{meas}$, were corrected using the experimentally derived relation:

$$TBED = 0.9384\ TBED_{meas} - 9.501\ (r = 0.969).$$

Reduction of the high voltage to $96KV_p$ showed that the correction depends on the photon spectrum.

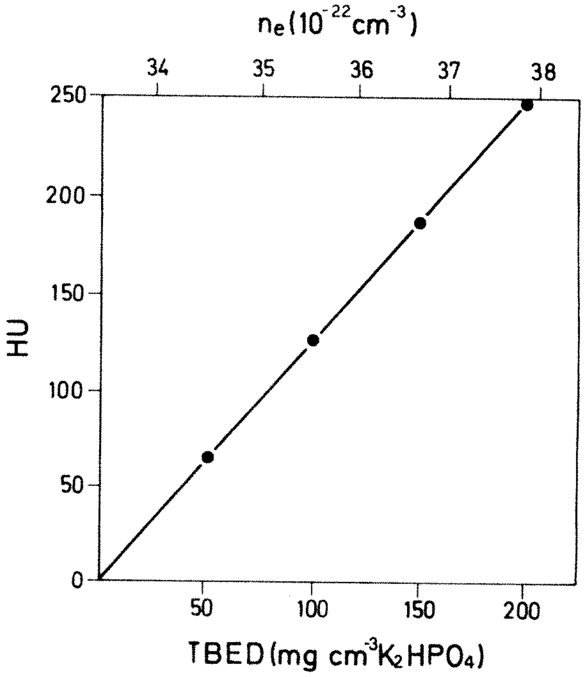

Figure 2. Dependence of the CT numbers (HU) on the concentration of the K_2HPO_4 solutions (TBED) and the electron volume density (n_e).

Subjects

Figures 3 and 4 show the trabecular bone equivalent density *versus* age by linear regression analysis including the tolerance intervals (90%). The corresponding coefficients of correlation were 0.75 and 0.77 for men and women, respectively ($p < 0.001$ in both cases). Applying exponential fitting, the coefficients of correlation were 0.73 and 0.75 for men and women, respectively. The residual variance for cubic fitting of the data for both

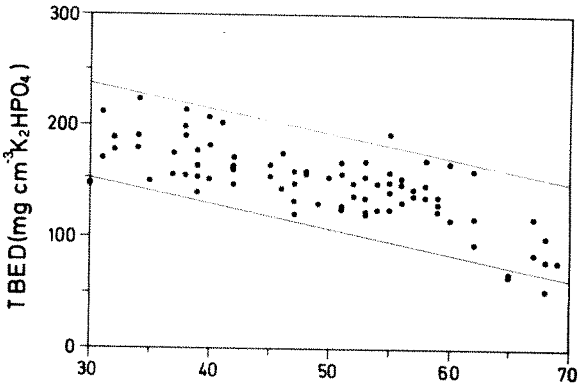

Figure 3. Dependence of the TBED values on age, for 84 normal Greek males (the lines indicate the 90% tolerance interval). According to linear regression analysis: TBED = 263.7-2.31A, $r = -0.75$ (TBED in mg cm^{-3} and A in years).

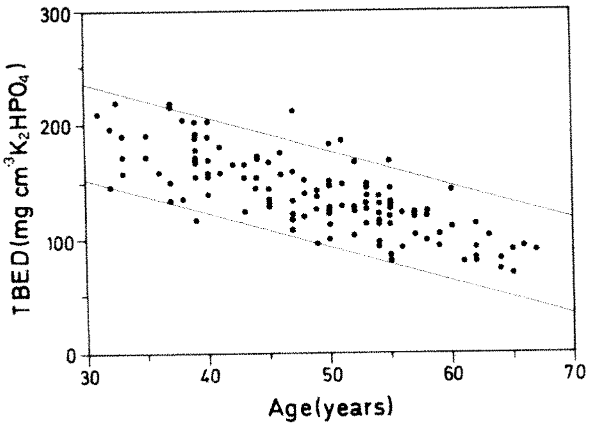

Figure 4. Dependence of the TBED values on age for 122 normal Greek females (the lines indicate the 90% tolerance interval). According to linear regression analysis: TBED = 285.5–2.90A, $r = -0.77$ (TBED in mg cm^{-3} and A in years).

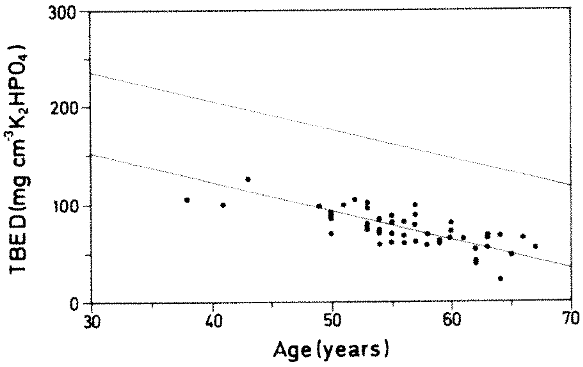

Figure 5. Dependence of the TBED values on age for 50 postmenopausal osteoporotic females. The lines indicate the 90% tolerance interval of the normal Greek females.

sexes was less than for the linear fit, but not significant ($p > 0.1$).

No correlation was found between the TBED values and the body habitus, milk consumption, smoking habits, and number of full-term pregnancies. The female normal population was divided in subgroups by applying the following criteria: (a) women older than ($n = 64$) and younger than ($n = 58$) 50 years, and (b) women before ($n = 61$) and after ($n = 61$) menopause (at least 6 months without menstruation). No significant difference in the rate of TBED annual loss was found between these subgroups. The application of the post-menopausal time instead of age for the postmenopausal women showed a significant difference in the TBED average annual loss between the perimenopausal women (6–36 months without menstruation, 8.45 mg cm^{-3}, $n = 22$) and women either before (2.38 mg cm^{-3}, $n = 61$), or at least 3 years after menopause (2.60 mg cm^{-3}, $n = 39$).

Reduced TBED values relative to sex and age matched controls were found in the groups of patients. The mean differences in TBED values between healthy and osteoporotic women was 30% ($p < 0.01$). Among the osteoporotic women, none had values greater than the mean value of the controls, and 45% showed TBED values below the fifth percentile (Fig. 5). This percentage increased to 72% when only women with vertebral fractures are considered. The average decrement, for the second group, consisting of alcoholic males, relative to matched controls, was 26%. The 12 gastrectomized males (Billroth II technique) of the third group, showed a significant decrement (30%) compared to controls.

An alternative analysis of the data on normal subjects was carried out considering separately each vertebra. The short-term *in vivo* precision was found to be 4.2 mg cm^{-3}, about 50% higher than the precision through the analysis of the data for all four vertebrae. The linear fitting of the data indicates that the average annual TBED loss is vertebra dependent (Table I).

Discussion

In the present study, various errors were investigated. A correcting factor for field non-uniformmity was applied in the TBED data that depends on the photon spectra. We believe that this finding, as well as the interscanner variability (Mostrom & Ytterbergh, 1988), suggests that normal data from local populations should be used for comparisons with data from patients. This approach also takes into account possible methodological differences which might exist between various research centres (Cann, 1987) as well as racial and geographic variations in bone mineral density.

The precision and the radiation burden of an *in vivo* examination are important factors to consider. The radiation burden of the patients undergoing the QCT

Table I. Age dependence of the average TBED (in mg cm^{-3} of K$_2$HPO$_4$) in the vertebral bodies of normal Greek subjects (A in years)

	Male		Female	
T_{12}	259.7–2.09A	$r = -0.67$	289.3–2.90A	$r = -0.73$
L_1	265.0–2.27A	$r = -0.73$	282.3–2.84A	$r = -0.74$
L_2	260.8–2.30A	$r = -0.75$	287.0–3.08A	$r = -0.77$
L_3	262.2–2.43A	$r = -0.77$	284.3–3.20A	$r = -0.77$
All	263.7–2.31A	$r = -0.75$	285.5–2.90A	$r = -0.77$

examination is significantly lower than that of radiographs of the thoracic and lumbar spine. The coefficient of variation for normal subjects ranges from 1.4% for men of 30 years to 3.0% for women of 65 years. These results are lower than those reported by Rosenthal et al (1985), who applied the single KV_p technique (2–3% for young adults) but similar to the findings of Genant et al (1987). The main sources of random error in QCT are the photon statistics, the selection of ROI, and the positioning of the patient. An increase in radiation burden does not substantially improve precision. Re-selection of the ROI had a minor influence on the *in vivo* precision and patient repositioning is the main source of error.

The TBED takes into account not only bone mineral and water but all the principle constituents of the trabecular part of the vertebra, *i.e.* calcium hydroxyapatite, collagen, red marrow and adipose tissue. Therefore, the term TBED was introduced in the present study, instead of the terms "bone mineral density" and "trabecular bone density" which are widely used in the literature.

It is well known that the percentage of the adipose tissue component increases with age, reducing the TBED values (Mazess & Vetter, 1985; Laval-Jeantet et al, 1986). Dual energy spectrum QCT techniques (Adams et al, 1982; Kalender et al, 1986) have been used to reduce this systematic error, which affects mainly the older population. However, the application of dual energy spectrum QCT with similar radiation burden on the patient reduces the precision (Wahner et al, 1984b; Nickoloff & Feldman, 1985). Moreover, according to Genant et al (1987) and Cann et al (1985a), dual energy spectrum technique does not enhance the discrimination between the normal and the osteoporotic women. In the present study, no corrections were made for age-related adipose tissue and collagen variations in the ROI. The overall accuracy of the single energy spectrum QCT technique, has been found to be 4–31% (Firooznia et al, 1984; Genant et al, 1987; Laval-Jeantet et al, 1986) using vertebrae from fresh cadavers with ages less than 69 years.

The simultaneous requirements for high precision and low radiation burden, as well as problems associated with the variation of fat with age, led us to apply the technique only on subjects aged 28–69 years. A tendency to a caudal spinal TBED reduction was found (Table I). This finding, which is in accordance with other studies (Singer & Breidahl, 1990; Thickman et al, 1990), needs further investigation. Asymptomatic males and females lose annually, on average, 2.3 mg cm^{-3} and 2.9 mg cm^{-3}, respectively, reducing their initial TBED value by 42% and 53% between 30 and 65 years. The fractional change in TBED found in the present study in Greek subjects is significantly higher than that reported by Firooznia et al (1984), Genant et al (1987), Ott et al (1987), and Compston et al (1988), but similar to that reported by Fujii et al (1987) and Doren et al (1987).

The rapid fractional change in spinal TBED with age is in contrast with the findings by Exner et al (1979) and Hesp et al (1985), who found that, in normal adults, the trabecular bone density in the distal radius is relatively constant until about 60 years of age. These differences might be attributed to varying trabecular bone alterations between forearm and spine.

No correlation was found between the TBED values and body height or weight, in accord with other investigators (Cann et al, 1985b; Banks & Stevenson 1986; Montag et al, 1987; Ott et al, 1987; Compston et al, 1988). In addition, there was no correlation between TBED values and milk consumption, smoking habits in men and number of full-term pregnancies.

The QCT technique has been used to predict osteoporotic fractures in women (Cann et al, 1985b; McBroom et al, 1985; Firooznia et al, 1986). Genant et al (1987) proposed a value of 110 mg cm^{-3} as the fracture threshold despite differences in techniques in different laboratories. The fracture threshold proposed by Firooznia et al (1986) is the fifth percentile on normal women of 45 years. Our results indicate that 92% of osteoporotic women exhibit TBED values lower than the fifth percentile of normal 45-year-old Greek women, and 96% of them exhibited TBED values lower than 110 mg cm^{-3}. However, among the 33 normal women 55–68 years old, 18 exhibited TBED values lower than 110 mg cm^{-3}.

Studies on osteoporotic women with mild to moderate vertebral compression fractures, showed average decrements, compared with normals, of 65% (Gallagher et al, 1985), 54% (Sambrook et al, 1985) and 36% (Reinbold et al, 1986). Reviewing only the women with osteoporotic fractures, we found a 42% decrement ($p < 0.001$). Among this group, 72% showed TBED values below the fifth percentile in women of the corresponding age. This result is comparable to the 64% reported by Firooznia et al (1986).

Hepatic osteodystrophy consists of osteoporosis and osteomalacia (Compston, 1986; Diamond et al, 1989). Alterations in bone mass in association with chronic liver disease have been well documented using other non-invasive techniques (Saville, 1965; Nilsson & Westlin, 1973; Kato et al, 1982). In the present study, the average decrement relative to matched controls was 26%. The 12 gastrectomized males (Billroth II technique) showed a significant decrement (30%) compared with controls. The low TBED observed in these patients could be attributed to vitamin D malabsorption (Nordin, 1983; Compston 1986; Krane & Holick, 1987).

Application of the technique in 73 patients with end-stage chronic renal failure (Kalef-Ezra et al, 1990) showed normal TBED values in non-dialysed patients, and reduced values in dialysed patients. Repeated measurements confirmed these findings.

In conclusion, a modified Cann–Genant QCT technique was developed, sources of error were investigated, and the corresponding dosimetric indices were obtained. The normal data concerning Greek adult subjects revealed an age-related bone loss. The data on various groups of patients confirmed the ability of QCT to provide a reliable means to evaluate alterations in spinal trabecular bone.

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Iliac insufficiency fractures

By A. M. Davies, FRCR and S. A. Bradley, FRCR

Department of Radiology, Royal Orthopaedic Hospital, Birmingham, UK

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Abstract. Twenty-five post-menopausal women with one or more insufficiency fractures of the pelvic ring are reported. In 80% of cases the fractures were multiple and a total of 79 insufficiency fractures was identified. Twelve iliac insufficiency fractures were present in 11 patients located at one of three sites: above and parallel to the acetabular roof ("supra-acetabular"), extending diagonally across the iliac ala from the greater sciatic notch ("oblique iliac"), and adjacent to the sacro-iliac joint ("superomedial iliac"). The plain radiographic appearances of these iliac fractures were typically subtle with ill defined medullary sclerosis, due to trabecular compression, the cardinal sign. Scintigraphy revealed the fractures as foci of increased activity which, in the presence of multiple pelvic insufficiency fractures, may be mistaken for metastatic disease. Computed tomography can be helpful in confirming the presence of suspected fractures, revealing further occult fractures and also excluding the likelihod of malignancy.

In the presence of osteoporosis the elastic resistance of bone is reduced, thereby predisposing it to the development of insufficiency fractures (Kroening & Shelton, 1963; Pentecost et al, 1964; Daffner, 1978). This form of stress fracture arising in the pelvis is particularly prevalent in the increasingly elderly population (Lodwick et al, 1987). The typical location for these pelvic fractures is the body of the pubis (parasymphyseal) and the sacral ala. The former are commonly mistaken for malignant lesions (Goergen et al, 1978; Casey et al, 1984; Hall et al, 1984; McGuigan et al, 1984), whereas the latter are often overlooked on plain radiography (Lourie, 1982; Reis, 1983; Schneider et al, 1984; Cooper et al, 1985a; Gaucher et al, 1987; Roucoulès et al, 1987). Fractures of both bones, parasymphyseal and sacral, frequently occur together (Cooper et al, 1985a; DeSmet & Neff, 1985; Davies et al, 1988). A less common site of involvement is the iliac bone, and insufficiency fractures have been reported in the blade of the ilium (Cooper et al, 1985a; Gaucher et al, 1986a,b; Davies et al, 1988) and rarely in the supra-acetabular portion (Cooper et al, 1985b; Gaucher et al, 1986c; Davies et al, 1988). The purpose of this paper is to report the radiological features of iliac insufficiency fractures identified in a series of patients presenting with insufficiency fractures of the pelvis.

Patients and methods

In a 5-year period, 25 patients with one or more insufficiency fractures of the pelvis were identified in our institution. Plain radiographs were available in all cases, scintigraphy in 11 and computed tomography (CT) in nine. Eleven of the cases, presenting with a parasymphyseal insufficiency fracture, have been previously reported (Davies et al, 1988). Isolated insufficiency fractures of the medial wall of the acetabulum have not been included in this series as they are relatively common.

Results

The clinical details of the 25 patients presenting with one or more insufficiency fractures of the pelvis are summarized in Table I. Cases 1–11 inclusive were all shown to have an iliac fracture whereas the remaining cases, 12–25, did not. All were post-menopausal women, aged 55 to 82 years (mean 70 years). The mean ages were similar for those with or without an iliac fracture. A total of 79 pelvic insufficiency fractures were identified, with a mean of 3.2 fractures per patient (range 1–7 fractures, Table I). Those cases with an iliac fracture had an average of one more fracture per patient than those without an iliac fracture.

On the plain radiographs all patients showed varying degrees of post-menopausal osteoporosis. Eleven patients (46%) had additional risk factors such as rheumatoid arthritis (seven patients), oral steroid therapy (two patients) and previous radiotherapy to the pelvis (two patients) (Table I). Only five patients gave a history of minor trauma prior to the onset of symptoms and in no case was this sufficient initially to immobilize the patient or require investigation. The commonest presenting complaints were low back pain and deep groin or hip pain.

The iliac insufficiency fractures were identified at three specific sites: above the roof of the acetabulum (supraacetabular, two patients), extending diagonally across the iliac ala (oblique iliac, five patients) and in the medial ilium adjacent to the sacro-iliac joint (superomedial, five patients). In only one case did an iliac fracture occur in the absence of other insufficiency fractures and in one patient two iliac fractures were present on the same side.

Address for correspondence: Dr A. M. Davies, Department of Radiology, Royal Orthopaedic Hospital, Woodlands, Northfield, Birmingham B31 2AP.

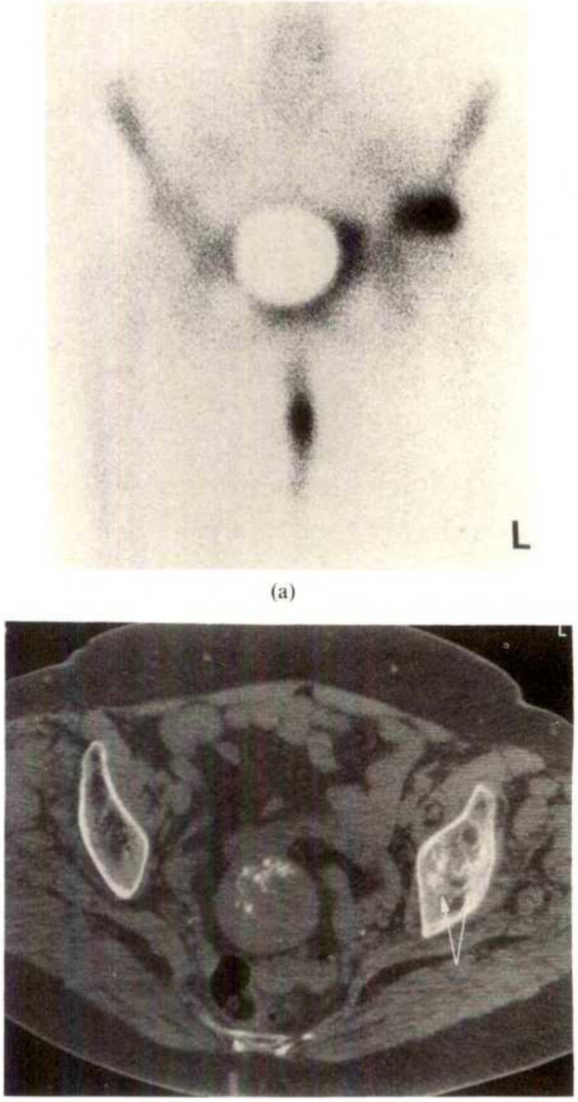
Table I. Clinical details and site of 79 pelvic insufficiency fractures in 25 post-menopausal women

Case	Age (years)	Trauma	Additional risk factors	Site of fractures
1	66		Rheumatoid	SA
2	82			OI, SPR (b), IPR (b), S (b)
3	63	+	Oral steroids	OI, P, SPR, IPR, A
4	78			OI, SA, S, P
5	83		Rheumatoid	SMI, S (b), P, A
6	77		Rheumatoid	OI, P
7	71			SMI, S (b), P
8	61		Radiotherapy	OI, S, P, A
9	73			SMI, S (b), P
10	70			SMI, P
11	55	+	Rheumatoid	SMI, S, P
12	79			P
13	69	+	Rheumatoid	P, IPR
14	71		Rheumatoid	P
15	68			P, IPR
16	68		Oral Steroids	P
17	62	+		S (b), P
18	63		Radiotherapy	S (b), P
19	66			S, P
20	65	+		P, IPR (b), SPR
21	73		Rheumatoid	P
22	76			S (b), P, SPR, IPR
23	68			S, P, SPR, IPR (b)
24	69			P, SPR, IPR (b)
25	70			P (b), S (b)

SA, supra-acetabular; OI, oblique iliac; SMI, superomedial iliac; P, parasymphyseal; SPR, superior pubic ramus; IPR, inferior pubic ramus; A, medial wall acetabulum; S, sacral; (b), bilateral fractures.

The supra-acetabular fractures were initially revealed by scintigraphy as small elliptical foci of increased activity located above and parallel to the roof of the acetabulum (Fig. 1a). On CT, ill defined medullary sclerosis, approximately 1 cm above the articular cortex of the acetabular roof, confirmed the presence of the fracture (Fig. 1b). Only subtle sclerosis subsequently developed at this site on the plain radiographs.

The oblique iliac fractures demonstrated two different patterns. Firstly, a broad band of medullary sclerosis, visible on both plain radiography and CT, commencing in the greater sciatic notch, level with the inferior aspect of the sacro-iliac joint and extending diagonally, superiorly, into the blade of the ilium (Figs 2a and 2b). Laterally the band of sclerosis is shown to taper to a point (Fig. 2a). Scintigraphy demonstrates a wedge-shaped area of increased activity corresponding to the site of the plain film and CT changes (Fig. 2c). The second form of oblique iliac fracture was seen as a subtle lucent fracture line extending diagonally across the iliac blade in a similar situation to the sclerotic variety (Fig. 3a). In this type, however, the fracture line extended laterally to the periphery of the ilium (Fig. 3a) and cortical disruption could be identified on CT (Fig. 3b).

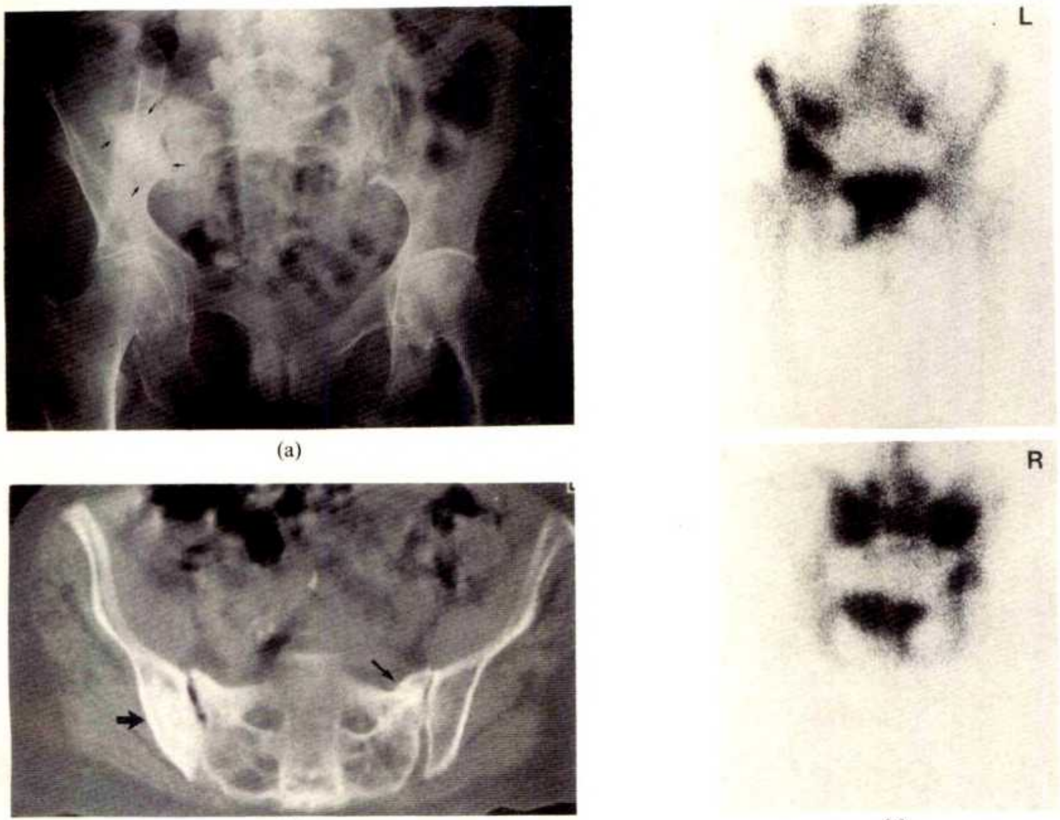


(a)

(b)

Figure 1. (a) Scintigraphy: 3 h anterior image of the pelvis revealing a left supra-acetabular fracture. (b) Axial CT: same case showing medullary sclerosis above the left acetabulum confirming the supra-acetabular fracture (arrowed).

Three of the superomedial iliac fractures were associated with bilateral sacral insufficiency fractures, one with an ipsilateral and one with a contralateral sacral fracture, and one with an intact sacrum. None of these superomedial iliac fractures could be clearly identified on the plain radiographs. Scintigraphy revealed increased activity at the site of the fractures shown best on the posterior image of the pelvis. Optimal demonstration of these fractures was with CT showing medullary sclerosis within the posterior aspect of the iliac bone immediately adjacent to the sacro-iliac joint (Figs 4a and 4b). The sacral fractures, where present,



(a)

(b)

(c)

Figure 2. (a) Radiograph showing a right parasymphyseal fracture and an oblique iliac fracture indicated by medullary sclerosis (arrowed). (b) Axial CT: same case showing medullary sclerosis in the right iliac bone adjacent to the SI joint due to the Iliac fracture (large arrow) and a fracture of the left sacral ala anteriorly (small arrow). Degenerate vacuum phenomenon in the right sacro-iliac joint. (c) Scintigraphy: 3 h anterior and posterior images of the pelvis showing foci of increased activity corresponding to the right iliac, left sacral, right supra-acetabular (not visible on 2a) and right parasymphyseal (partially obscured by bladder activity) insufficiency fractures.

were also ideally demonstrated by CT (Figs 2b, 3b, 4a and 4b).

Sacral insufficiency fractures were present in a total of 13 cases of which seven (54%) were associated with either superomedial or oblique iliac insufficiency fractures (Figs 2b, 3b and 4b).

Discussion

Insufficiency fractures of the pelvis and sacrum, as in this series, are diagnoses confined almost exclusively to post-menopausal women. Other predisposing factors, present in almost half the patients in this study, include rheumatoid arthritis, steroid therapy and previous pelvic irradiation (Taylor et al, 1971; DeSmet & Neff, 1985). The clinical manifestations are often non-specific, and, without a history of trauma, other diagnoses may be considered. The radiographic manifestations may also be problematic, being subtle in the case of sacral fractures (Lourie, 1982; Reis, 1983; Schneider et al, 1984; Gaucher et al, 1987; Roucoulès et al, 1987) and diagnostically misleading in the case of parasymphyseal insufficiency fractures (Goergen et al, 1978; Casey et al, 1984; Hall et al, 1984; McGuigan et al, 1984; Davies et al, 1988).

Further confusion may occur when spontaneous insufficiency fractures arise at multiple sites including the ilium (Figs 2a and 3a). Although iliac insufficiency fractures have long been recognized (Taylor et al, 1971), those involving the blade of the ilium have received little attention (Cooper et al, 1985a). Medullary sclerosis of an oblique iliac insufficiency fracture may be indistinguishable from radionecrosis of bone. If, however, the dose to the affected bone is less than 4000 rads, then a fracture secondary to radiation bone atrophy is more likely than necrosis (Kim et al, 1974; Howland et al, 1975).

Supra-acetabular fractures are rare in comparison with those involving the medial wall of the acetabulum which is a particularly common site in patients with rheumatoid arthritis. The two cases in the current study were both revealed by scintigraphy (Figs 1a and 2c) and confirmed by CT (Fig. 1b) although radiographic find-

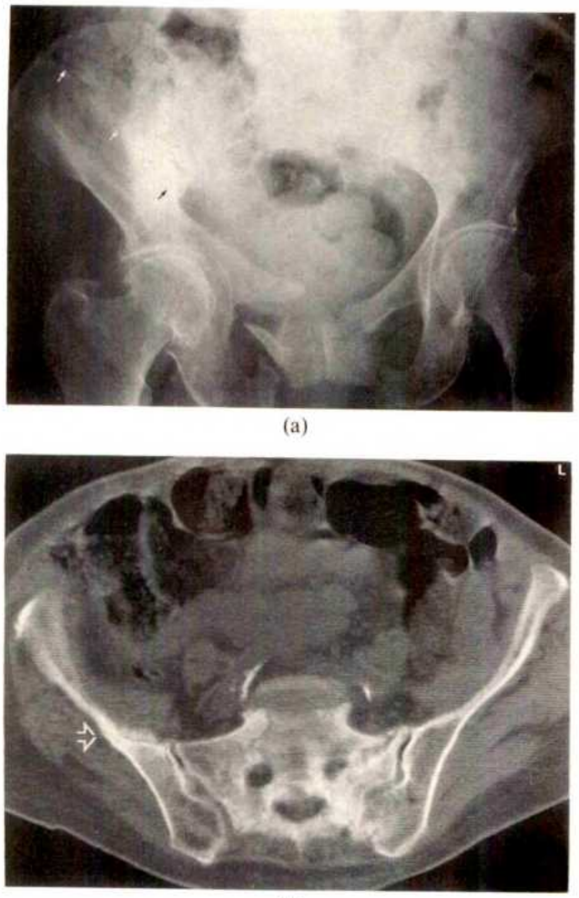


Figure 3. (a) Radiograph showing multiple displaced pubic fractures and an oblique linear fracture of the right ilium (arrowed). (b) Axial CT: Same case showing cortical disruption of the right iliac fracture (arrowed) and bilateral sacral insufficiency fractures (not visible on 3a).

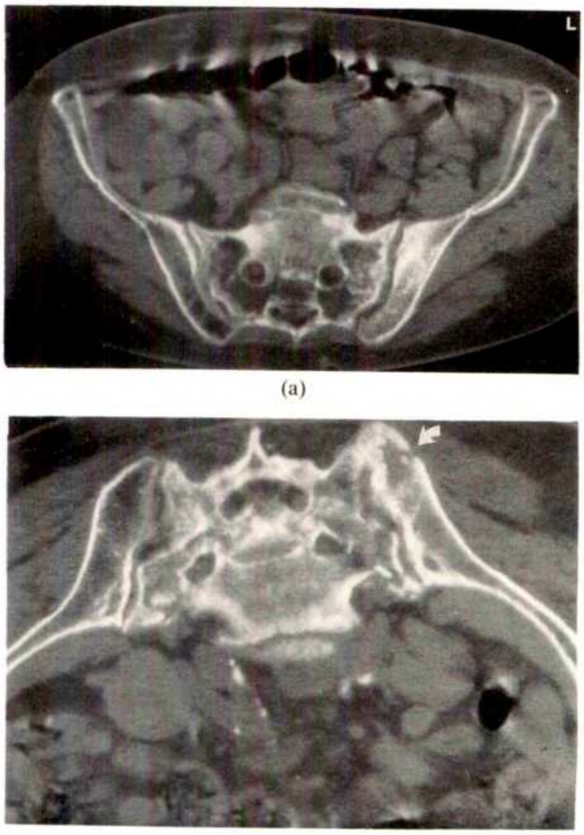


Figure 4. (a) Axial CT showing a left superomedial iliac insufficiency fracture indicated by the medullary sclerosis. The sacrum is intact. (b) Axial CT showing bilateral sacral fractures with involvement of the posterior aspect of the right superomedial iliac bone (arrowed).

ings of a hazy band of sclerosis located immediately above and parallel to the acetabular roof have been described (Cooper et al, 1985b; Gaucher et al, 1986c, 1987).

The third variety of iliac insufficiency fracture described in this study, the superomedial fracture (Fig. 4), has not been previously reported in the English literature. The medullary sclerosis with or without cortical disruption immediately adjacent to the sacro-iliac joint is best demonstrated by CT (Fig. 4). Although a similar appearance has been previously attributed to radiation bone changes (Raffii et al, 1988), it is likely that it represents a fracture as none of the five cases in this study had undergone pelvic irradiation. The mechanism of injury is presumably identical to that inducing the sacral fractures, with stress being applied vertically to the sacral ala, across the sacro-iliac joints and into the posteromedial aspect of the upper ilium. The characteristic scintigraphic appearance of bilateral sacral insufficiency fractures is the so-called H-shaped pattern (Reis, 1983; Schneider et al, 1984; Davies et al, 1988). Any distortion of this configuration should alert the radiologist to the possibility of superomedial iliac involvement.

To distinguish between insufficiency fractures of the blade and superomedial ilium is somewhat artificial as the medullary sclerosis in some cases of the oblique variety commences medially in the ilium adjacent to the sacro-iliac joint (Figs 2a and 2b) (Cooper et al, 1985b). In this situation, however, both scintigraphy and CT will demonstrate the more pronounced involvement of the iliac ala in the oblique type (Figs 2b and 2c).

As with many insufficiency fractures, the oblique orientation in the iliac bone is a typical location for Looser's zones of metabolic bone disease (Gaucher et al, 1986b). Whilst it is generally accepted that it is stress due to undue loading of weakened bone that leads to insufficiency fracture formation (Pentecost et al, 1964), some have suggested that Looser's zones in the iliac blade are precipitated by arterial pulsations of the superior gluteal artery (Griffin, 1982). It seems probable, however, that as the sites of the three types of iliac insufficiency fracture described above correspond to the approximate location of the inferior, middle and posterior gluteal lines, the gluteal muscles have a role in the pathogenesis of these fractures.

In a post-menopausal woman presenting with low back, pelvic or hip pain, a careful search for the subtle radiographic signs of an insufficiency fracture of the pelvic ring should be made (Davies et al, 1988). As many cases are multiple (Table I), scintigraphy will reveal the full extent of the fractures (Fig. 2c). Care should be taken not to interpret multiple foci of increased activity as indicative of metastases. Computed tomography, whilst not always necessary, will confirm the presence of an insufficiency fracture and exclude the diagnosis of metastatic disease (Figs 1b, 2b, 3b and 4).

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Computed tomography of cranial metastatic malignant melanoma: features, early detection and unusual cases

By G. M. McGann, FRCS Ed, FRCR and A. Platts, FRCS, FRCR

Department of Radiology, Westminster Hospital, Page Street, London SW3, UK

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Abstract. The cranial computed tomographic (CT) scans reported as showing metastatic disease in patients with malignant melanoma (MM) seen at the Westminster Hospital over a 5 year period were reviewed. Ninety-eight patients with intracranial metastatic MM were identified. Twelve had an initial scan which was reported as normal and particular attention was given to these to see if, in retrospect, any early features of metastatic disease were discernible. Fifty-eight cases showed the "typical" features of intracranial MM; the remainder were unusual in appearance, behaviour, or site. Radiological regression was shown in only seven cases on follow-up scans; all but one of these patients had one or two large metastases. No significant lesion was thought to have been missed on a scan after the administration of intravenous contrast medium, but the lesions of three patients were difficult to discern on plain scans. Thus when MM metastasis is suspected, the use of the contrast-only scan is advocated.

The prevalence of malignant melanoma (MM) in the Western World has risen rapidly over the past few decades and is now 6 per 100 000 in the United States (Ackerman & Del Regato, 1985). Melanoma accounts for 1% of all malignancies, but, after breast and bronchus, it is the most common tumour metastasizing to the central nervous system (CNS) (Amer et al, 1978). Animal models have consistently confirmed the affinity of experimental melanoma metastases for the CNS (Brunson et al, 1978), though the reason for this is not known. The reported rate of CNS metastasis varies from 8% (Bullard et al, 1981) to 46% (Amer et al, 1978) depending on the clinical stage of the group of patients evaluated and the thickness and site of the primary tumour. Patients with advanced disease, with thicker primaries or those with head and neck lesions show a higher rate (Bullard et al, 1981). More recent series appear to show a higher rate of CNS spread, perhaps due to investigation of asymptomatic patients or to more aggressive treatment lengthening survival, although this issue is contentious (Das Gupta & Brasfield, 1964; Amer et al, 1978; Lee, 1983). The aim of this study was to catalogue the features of intracranial metastatic MM with a view to identifying its very earliest features, to assist in differential diagnosis in patients whose scan shows the features of intracranial metastases but no primary has yet been found, and to define the role of contrast enhancement.

Methods

A total of 312 patients with histologically confirmed MM underwent cranial computed tomography (CT) at the Westminster Hospital from 1983 to 1988 either for suspected intracranial metastases, or, in much smaller numbers, for screening purposes before the commencement of a clinical trial. The films or reports of 71 patients were either lost, damaged by fire or transferred to other hospitals and so were excluded from the study. Information was available on 241 patients. Those scans reported as showing abnormalities were reviewed by a single radiologist (G.M.). Features thought to represent intracranial metastatic MM were detected in 98 and abnormalities considered to represent areas of cerebral infarction were detected in three. The scans of four patients showed "equivocal" abnormalities which were not confirmed as metastatic by follow-up studies or, when available, by histology before or after death and were thus considered to be negative for intracranial metastatic MM. Those scans which were reported as normal, subsequently becoming abnormal, were given particular attention, especially areas of the scan in which metastases later developed, to determine if subtle early changes were present and if they were, whether they had different characteristics. The scans were performed on either an Elscint 905 or an Elscint 2400 system using 5 mm contiguous sections through the posterior fossa and 10 mm sections for the remainder. Eighty-one patients had both pre-contrast and post-contrast medium scans, with either a mixture of sodium and methylglucamine diatrizoate or iopamidol. A dose of approximately 300 mg of iodine per kilogram of body weight was used and scanning was performed without delay after intravenous administration.

Results

Ninety-eight (40.7%) of 241 patients underwent one or more scans which showed features of intracranial metastasis from their known primary MM. The lesions were classified as follows: single or multiple; large (greater than 2 cm in diameter) or small; high, low,

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Address for correspondence (both authors): Department of Radiology, Royal Free Hospital, Pond Street, London NW3, UK.

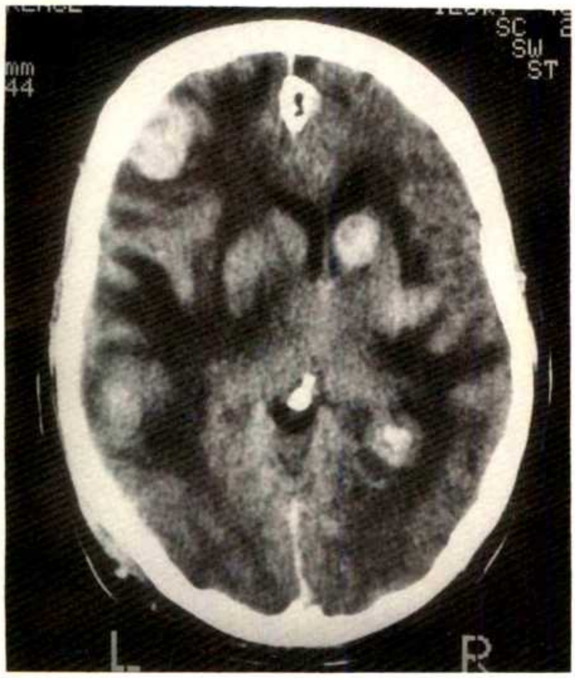


Figure 1. Typical melanoma metastases shown on enhanced axial CT.

Table I. Characteristics of intra-axial metastases ($N = 89$)

Characteristics		Number of patients	Percentage
Number	Single	32	36
	Multiple	57	64
Size	Small	53	59.6
	Large	23	25.8
	Both	13	14.6
Attenuation in relation to brain before contrast medium	High	76	85.4
	Low	1	1.1
	Isodense	5	5.6
	Mixed	7	7.9
Contour	Nodular	80	89.9
	Irregular	9	10.1

isodense or mixed attenuation pre-contrast compared with surrounding brain substance. Intra-axial metastases were classified as cerebral, cerebellar or brainstem. Evidence of extra-axial metatases was also noted. Oedema was graded as marked, mild or none. The majority of these patients had metastatic disease elsewhere, and many underwent subsequent scanning showing progression in number or size of the lesions. Typical melanoma metastases were taken to be single or multiple nodules in brain parenchyma of high attenuation showing surrounding oedema and enhancement after contrast medium administration. Eighty-nine patients (90.8%) had lesions confined to brain parenchyma, 58 patients (59.2%) had "typical" metastases (Fig. 1).

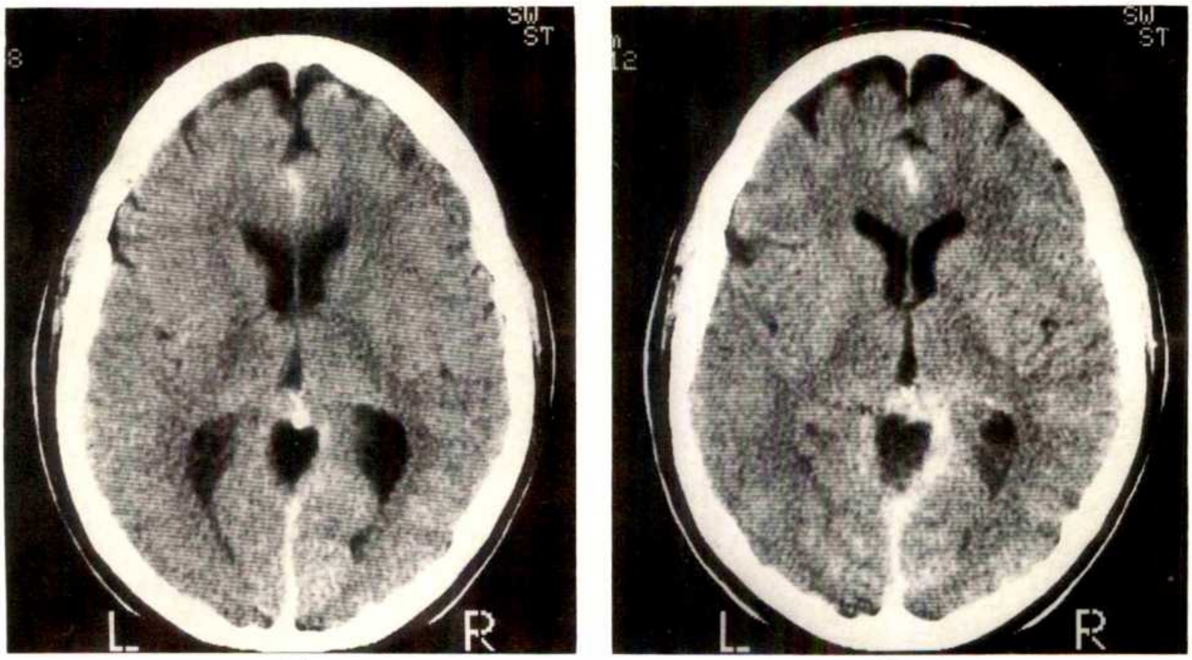
The majority (64%) of the patients with abnormal scans had multiple lesions (see Table I). Fifty-three patients (59.6%) had small lesions only, 13 (14.6%) had both small and large lesions. High attenuation was a feature in 76 patients (85.4%), seven cases showed mixed high and low attenuation, five were isodense, one was hypodense. Eighty patients (89.9%) had nodular lesions, 73 (82%) showed surrounding oedema. Of those patients who had both pre-contrast and post-contrast medium studies, only one patient who had several hyperdense nodules failed to enhance. Three patients showed isodense lesions which enhanced after contrast medium. Enhancement was relatively uniform in 73 patients and peripheral (ring-like) in seven. The lesions were confined to cerebral substance in 75 cases (76.5%), and were both cerebral and cerebellar in 14. No patient had metastases confined to the cerebellum.

Twelve patients with features of intracranial metastatic MM had undergone previous scans reported as normal. Their initial studies were performed between 1 and 24 months (average 9.4 months) before their abnormal study. On review of the initial scans, abnormalities were detected in the studies of four patients at sites which later became unequivocally abnormal. The scans of two patients showed small areas of low attenuation with no abnormal enhancement. None of the abnormalities would have justified an unequivocal report of metastasis at the earlier stage.

Discrete metastases apparently occupying the subarachnoid spaces were seen in five patients. In a further five there was evidence of diffuse meningeal involvement, of whom three showed additional intra-axial lesions and one showed spinal lesions. Table II lists unusual sites of metastasis and their frequency. Six patients developed hydrocephalus, due in three of them to direct compression of the fourth ventricle by a cerebellar metastasis. The other three showed "communicating" hydrocephalus. Meningeal infiltration was shown as marked meningeal enhancement in one of these patients (Fig. 2), while two who had initial scans

Table II. Sites of unusual metastasis

Site	Number of patients
Diffuse meningeal	5
Tentorial edge nodule	2
Orbits	2
Corpus callosum	5
Superior vermis	2
Skull vault	3
Ependyma (IIIrd ventricle)	1
Midbrain cistern	1
Cerebellopontine angle	1



(a) (b)

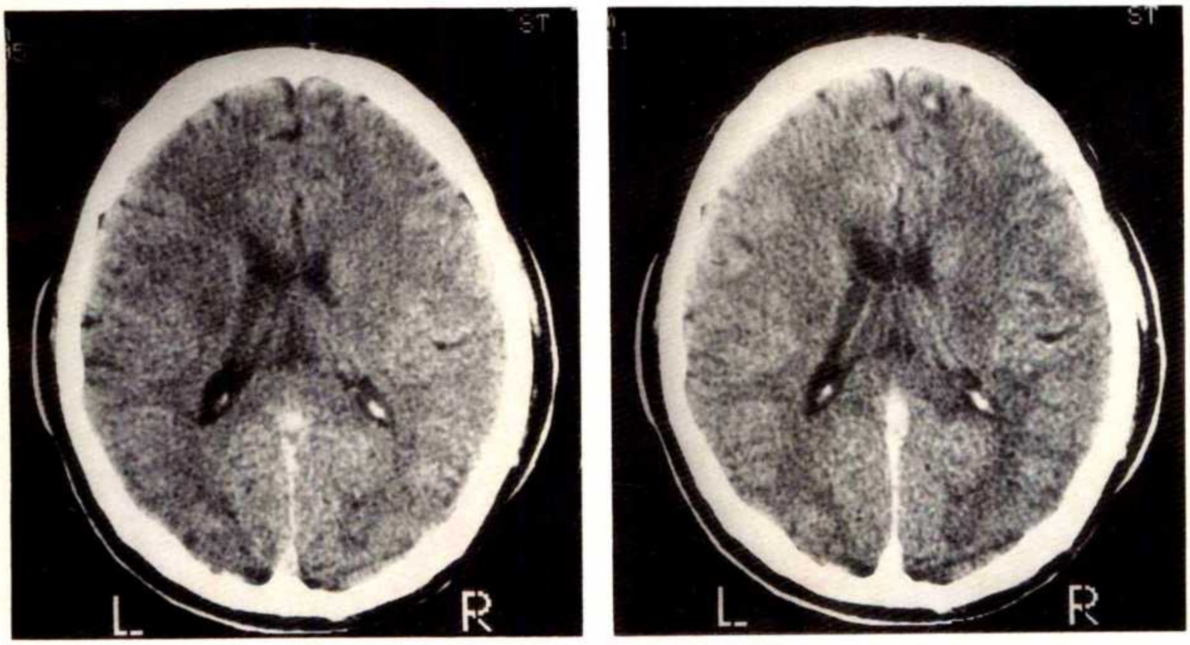
Figure 2. Axial CT (a) before and (b) after contrast medium showing meningeal enhancement, particularly around the falx cerebri and tentorial edge, indicating diffuse meningeal infiltration by metastatic melanoma.

showing no other abnormality later developed intra-axial deposits. Diminution in the size of lesions occurred in seven patients, all receiving steroids and chemotherapy: in six patients the lesions were large and showed a reduction in size; the other showed an apparent decrease in the number of small metastases.

Discussion

Patients presenting with primary MM in whom there is no evidence of metastasis either clinically or microscopically in regional lymph nodes have a 5 year survival greater than 60% (Ackerman & Del Regato, 1985). Zartman et al (1987) studied 90 such patients with a variety of investigations, including cranial CT, and finding no evidence of metastasis, concluded that these tests, in this group, were no more useful than a history and physical examination. Computed tomography has a more important role in advanced melanoma. The small number of patients with evidence of distal metastasis when first seen are likely to survive between 18 and 24 months. This figure falls to less than 5 months when intracranial metastasis is diagnosed (Ginaldi et al, 1981; Retsas & Gershuny, 1988). There are, however, some long term survivors; in a series of 72 patients with intracranial metastatic melanoma, Ziegler and Cooper (1986) reported a mean survival of 6.1 months for those with multiple lesions, 10.4 months with solitary lesions and 17.1 months after craniotomy and resection of a solitary lesion. Retsas and Gershuny (1988) reported four patients surviving over 2 years, with one disease-free at 82 months. So, although treatment for intracranial metastasis is usually palliative, one of the roles of CT scanning is to detect the potentially resectable solitary lesion. In our series, five patients underwent craniotomy. The longest survivor died 9 months after operation from a single recurrence under the craniotomy flap. The other four patients died from multiple metastases less than 8 months after operation. Radiological regression was only shown in seven patients, six of whom had one or two large metastases; this group may be more sensitive to treatment. It is also possible that diminution in size is mainly due to the effect of steroids and the resorption of haemorrhage.

In view of the aggressive nature of intracranial melanoma metastases, early diagnosis may not improve survival but it is important in prognosis. It has also been suggested that if cerebral metastases are present, certain chemotherapeutic regimes may be harmful (Holtas & Cronqvist, 1981), but this is a view which is not generally held. The data from this study show that intracranial spread from melanoma is likely to be manifest as multiple small nodules of high attenuation showing enhancement after contrast medium administration, in accordance with a previous slightly smaller series (Ginaldi et al, 1981). Bullard et al (1981) in a series of 107 cranial MM metastases found the solitary lesion (56.7%) to be more common than multiple lesions. Not all of their patients, however, underwent CT and the relative insensitivity of isotope scanning may account for this finding. From our data, a single intracranial lesion which is hypodense and does not show enhancement after contrast medium administra-



(a) (b)

Figure 3. (a) A small isodense right frontal metastasis, inconspicuous on the plain scan. (b) After contrast medium, the metastasis enhances and is now easily seen, as is a little surrounding oedema.

tion is very unlikely to be a melanoma metastasis, particularly if it lies within the cerebellum. As in other studies, meningeal involvement was demonstrated relatively infrequently (Ginaldi et al, 1981; Weisberg, 1985) although it was found in over 50% at autopsy (Amer et al, 1978). Although leptomeningeal involvement appears more frequent and more readily demonstrated on CT in leukaemia and lymphoma (Lee et al, 1984), nonetheless, hydrocephalus in a patient with melanoma should be considered to be due to intracranial metastasis until proven otherwise. Three patients had metastases which were isodense and difficult to discern on the plain scan (Fig. 3). Only one patient had unenhancing lesions, but these were hyperdense and diagnosable on both the plain and enhanced scans. Thus when melanoma metastases are suspected, an enhanced-only scan is sufficient for their detection. When it is important to elucidate haemorrhage, which is a frequent occurrence in metastatic cranial MM, a plain scan could be carried out subsequently.

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The most advantageous timing of external ureteric compression during intravenous urography

By T. H. Hughes, FRCSEd and A. L. Hine, MRCP, FRCR

Department of Radiology, Central Middlesex Hospital, Acton Lane, Park Royal, London NW10 7NS, UK

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Abstract. The objective of this study was to ascertain the most advantageous time during an intravenous urogram to apply external ureteric compression to gain the greatest calyceal distension. This was a prospective randomized trial of 60 patients, divided into three equal groups with compression applied immediately after injection, at 5 minutes and after the 5 minute film had been viewed. Patients with the usual criteria for avoiding compression were excluded. A statistically significant improvement in calyceal distension occurred when compression was applied at 5 minutes compared with that applied after the 5 minute film had been viewed. No improvement was seen when the compression was applied immediately after injection. We recommend that external ureteric compression should be applied immediately after the 5 minute film.

External ureteric compression became popular shortly after the introduction of excretory urography (Ziegler, 1930). Other techniques include placing the patient in Trendelenburg or using bladder distension (Braasch, 1931). Compression became routine following an early uncompressed film (Kornblum, 1932), with the exclusion of the following groups of patients: painful or tender abdomen, palpable abdominal mass, known abdominal aortic aneurysm, symptoms of ureteric colic, renal failure, age under 12 years, recent surgery and if a limited intravenous urogram (IVU) is indicated. Many reports have since confirmed the value of compression (Beare & Wattenberg, 1950; Harrow & Sloane, 1963; Hamby & Kirsh, 1964; Heetderks et al, 1964; Cimmino, 1965; Powell et al, 1967; Mawhinney & Gregson, 1987). Two main types of apparatus have been described for compression (Steinert, 1952; Eklof, 1965), those that wrap around the patient and allow oblique views and those that attach to the table and prevent patient movement. They have been shown to be equally effective (Daughtridge, 1965). There is no firm agreement as to the most advantageous timing of compression which can vary from immediately after injection (Hattery et al, 1988), immediately after the 5 minute film (Ford & Palubinskas, 1967), or waiting until after the 5 minute film has been viewed (Cattell et al, 1989).

Patients and methods

A prospective randomized study was performed. All patients referred for non-emergency IVUs were considered (112 patients) but some were excluded from the trial on the following grounds (52 patients): tender or painful abdomen (five), palpable abdominal mass (two), only one kidney present (three), ultrasound as preferred investigation (five), upper tenth centile for weight (10), symptoms of ureteric colic (18), renal failure (three), follow-up limited IVUs (six). The remaining 60 patients were randomly assigned to one of three groups of 20:

(A) compression applied immediately after injection and the exposure of the nephrogram;

(B) compression applied at 5 minutes;

(C) compression applied after the 5 minute film had been viewed.

All IVUs and the application of external ureteric compression were performed by one radiologist (T.H.). All patients had the departmental standard preparation. The compression device was of the type attached to the table, using a ratchet and band, with foam pads below the band. All patients received 1 ml of iopamidol (Niopam 300 mg/ml) per kilogram. Films were taken immediately, at 5 minutes and at 10 minutes, following contrast medium injection. The examination proceeded normally, with further techniques such as obliques, tomography or second injection as necessary. The distension of the calyceal system for each kidney on the 10 minute film was scored independently by two radiologists unaware of when the compression was applied, using a standard scoring system (Mawhinney & Gregson, 1987) (Fig. 1). Statistical analysis was performed using the χ^2 test. The time at which the 5 minute film became available for viewing was recorded and was immediately seen by the radiologist (T.H.). Film processing was by a 90 second daylight processor.

Results

The compression results at 10 minutes are shown in Fig. 2 and the mean value and 95% confidence limits in Table I. This shows a statistically significant improvement ($p < 0.05$) in the scores 1 and 2 against 3 and 4 in calyceal dilatation if the compression is applied immediately after the 5 minute film rather than waiting for the 5 minute film to be viewed. There is also a trend towards improved distension when compression is applied immediately after injection compared with that after the

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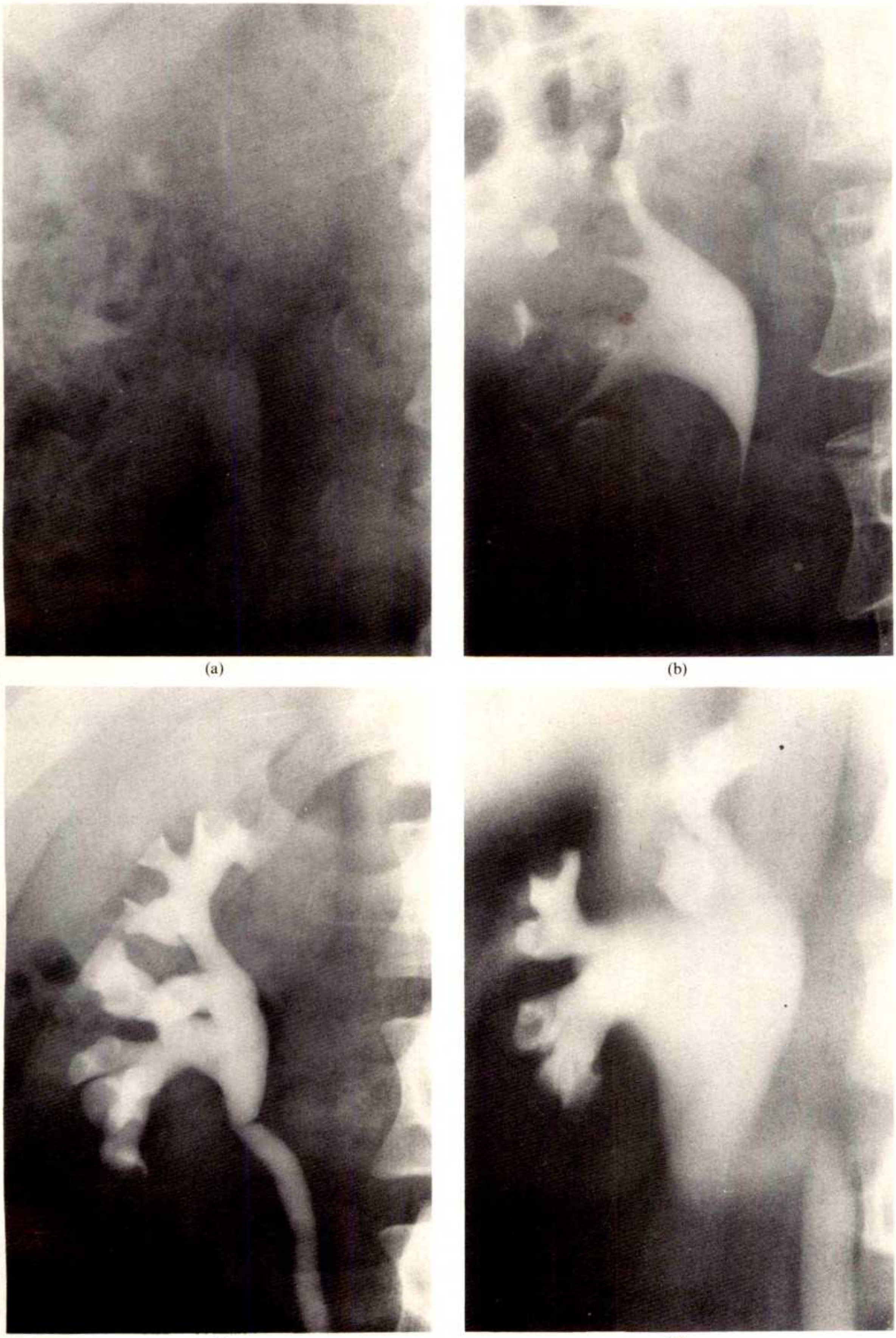
Address corrrespondence to: Dr T. H. Hughes, Department of Radiology, The Middlesex Hospital, Mortimer Street, London W1N 8AA, UK.



(a) (b) (c) (d)

Figure 1. Standard radiographs for assessing calyceal distension: (a) score 1, (b) score 2, (c) score 3, (d) score 4.

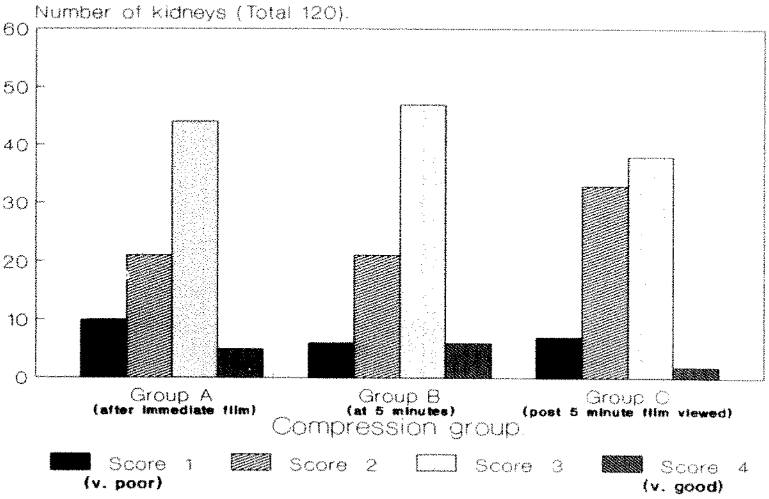


Figure 2. Compression results in the three groups.

5 minute film has been viewed, but this was not statistically significant. Interobserver agreement was 74% (Fig. 3). Although the interkidney agreement (same patient, right versus left) was 55%, those that disagreed were skewed positively to the right (Fig. 4). The average time from the taking of the 5 minute film to it being available for viewing was 3.8 minutes (range 2–8 minutes).

Discussion

Recent evidence (Mawhinney & Gregson, 1987) shows that compression is beneficial and in our study compression applied immediately after the 5 minute film gives better distension of the calyceal system than waiting for the 5 minute film to be viewed. Applying compression after the immediate film resulted in no additional improvement in distension. These results were obtained in the best possible situation where the radiologist was immediately on hand to view the 5 minute film, an average of 3.8 minutes later, using a 90 second processor. Without compression the distension is greater at 10 minutes than 15 minutes (Mawhinney & Gregson, 1987) and the most useful films are taken within 15 minutes of injection (Davidson, 1985), indicating that further delay in applying compression is likely to reduce its benefit. We recommend the following IVU sequence: the 5 minute film is taken to show physiological distension, then compression is applied immediately. The 5 minute film is then viewed and if compression is found to be undesirable (no case in our study) it can be removed, or indeed applied if avoided unnecessarily in the first place, for instance in the case of clinical ureteric obstruction not shown on IVU. Our study confirms the earlier finding (Berger, 1937) that the

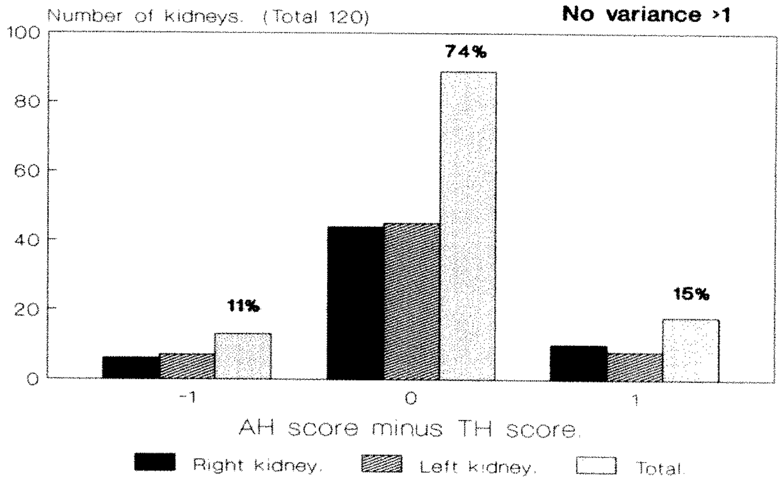


Figure 3. Inter-observer variance.

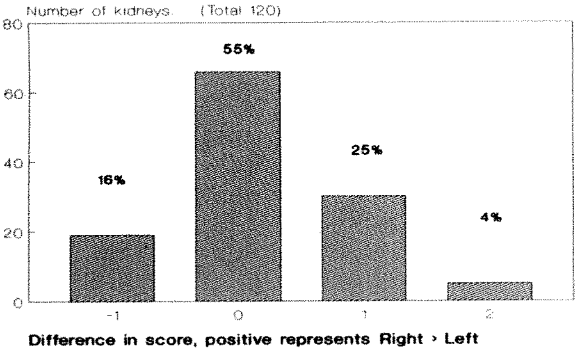


Figure 4. Graph showing the variance in the degree of calyceal distension between right and left kidneys in the same patient.

Table 1. 95% confidence limits for the degree of calyceal distension in the three groups

Group	Mean score (1–4)	95% confidence limits
A	2.55	2.41–2.69
B	2.65	2.54–2.76
C	2.44	2.33–2.54

left ureter could not be compressed as well as the right ureter, probably owing to the overlying sigmoid mesocolon.

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Use of percutaneous nephrostomy in malignant ureteric obstruction

By M. E. Chapman, MRCP, DMRD and J. H. Reid, DMRD, FRCR

Department of Diagnostic Radiology, Edinburgh Royal Infirmary, Edinburgh, UK

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Keywords: Percutaneous nephrostomy, Renal failure, Ureteric obstruction

Abstract. Seventeen patients with malignant disease underwent percutaneous nephrostomy to relieve renal failure secondary to ureteric obstruction. Renal function improved in 88%. The median survival time was 18 weeks and 58% left the primary hospital to return home or to a terminal care hospice. Minor complications occurred in 58%. The use of bilateral nephrostomy tubes conferred no greater benefit than a unilateral tube. Intervention in malignant ureteric obstruction may confer some benefit and should not necessarily be viewed with pessimism.

Percutaneous nephrostomy is a well established, relatively safe procedure which effectively improves renal function in obstructed kidneys (Keidan et al, 1988). Its use in malignant ureteric obstruction is a contentious issue because of the poor prognosis in this group of patients (Hepperle et al, 1979; Holden et al, 1979; Keidan et al, 1988). There are few studies on the use of percutaneous nephrostomy in this situation, the most recent by Keidan et al (1988). The lack of data contributes to the continued speculation as to whether this procedure is worthwhile or merely prolongs suffering.

In this study, the effect on renal function of unilateral or bilateral drainage, the complications, survival and quality of life of patients with malignant disease who underwent percutaneous nephrostomy for ureteric obstruction are assessed.

Methods

Seventeen patients who underwent percutaneous nephrostomy in a 5 year period between 1984 and 1989 at the Edinburgh Royal Infirmary were analysed retrospectively. All the patients presented with renal failure and bilateral ureteric obstruction. Each patient had either a single or bilateral nephrostomy tube with either an 8 or 10 FG pigtail catheter. The diagnosis, effect on renal function, complications and survival time were noted. Where a patient was either at home or in a hospice with a tube *in situ*, a questionnaire was sent to the General Practitioner or attendant physician to obtain further information on the quality of the patient's life.

The nephrostomy tubes were all inserted in the Radiology Department under local anaesthesia usually by combined ultrasonic and fluoroscopic guidance.

Results

There were 12 female and five male patients (see Table I). The sites of primary malignancy were three bladder, six cervical, two colon, one ovary, one bronchus, one oesophageal, one prostate and two breast. Twelve patients had a primary pelvic malignancy and in five patients distant retroperitoneal metastatic disease was responsible for the ureteric obstruction.

Five patients presented without a history suggesting malignancy. In five the renal failure and malignancy were diagnosed concurrently. In a further five a distant primary was known, but the cause of ureteric obstruction, subsequently shown to be metastatic ureteric involvement, was not known at the time of nephrostomy. Two patients with previous pelvic malignancy, cervical in each, re-presented with acute renal failure, one with recurrent local disease and the other with probable radiation fibrosis.

Improved renal function occurred in 15 (88%) with a return to normal blood urea levels within 10 days. There was no significant difference in the time to achieve this between patients with single or bilateral nephrostomy tubes (as assessed by the Wilcoxon rank sum test). Ureteric stents were subsequently inserted in four patients. Ten patients (58%) experienced minor complications which included minor sepsis, leaking, local inflammation and uncomplicated pelvic rupture.

Two patients (12%) had major complications, one with serious local superficial infection and a second with pyonephrosis. The tube was changed in seven patients, usually owing to the tube being inadvertently dislodged.

Survival data were analysed for 15 patients (survival data are not known for two patients). Three patients are still alive. These patients (two cervical and one prostate carcinoma) no longer have nephrostomy tubes *in situ*. Two have ureteric stents and well controlled disease. In the remainder, survival ranged from 4 weeks to 32 weeks with a median survival of 18 weeks. In the five patients with primary disease outside the pelvis, the median survival time, 16 weeks, was less. Four patients died at home and five in a local hospice, all with nephrostomy tubes *in situ*. Three patients died in hospital.

In those patients managed by nephrostomy outside the primary hospital, there was one major complication,

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Address correspondence to Dr M. E. Chapman. Current address: Edinburgh Royal Infirmary, Lauriston Place, Edinburgh, UK.

Table I. Summary of results

Number	Sex	Primary site	Number of nephrostomy tubes	Improved function	Survival time (weeks)	Place of death
1	M	Bladder	1	No	4	Hospital
2	M	Bladder	2	Yes	28	Home
3	F	Cervical	1	Yes	16	Hospice
4	F	Colon	1	Yes	32	Hospice
5	F	Cervical	2	Yes	Alive	—
6	F	Ovary	2	Yes	32	Home
7	M	Bronchus	2	Yes	28	Home
8	F	Colon	2	Yes	NK	—
9	F	Cervical	1	Yes	20	Hospital
10	F	Cervical	2	Yes	NK	—[a]
11	F	Oesophagus	2	Yes	8	Hospital
12	M	Prostate	1	Yes	Alive	—
13	F	Cervical	1	Yes	Alive	—
14	F	Breast	1	Yes	16	Home
15	M	Bladder	2	Yes	20	Hospice
16	F	Cervical	1	No	12	Hospice
17	F	Breast	2	Yes	16	Hospice

NK, not known.
[a] Lost to follow-up.

local sepsis. One patient complained of poor sleep because of the need for frequent bag emptying and another was afraid to leave the house in case the tube fell out. The remainder had no reported problems.

Discussion

Urinary diversion in malignant disease presents a therapeutic dilemma. Before the advent of percutaneous nephrostomy, the high complication rates of surgical urinary diversion weighed against intervention (Hepperle et al, 1979). However, percutaneous nephrostomy is relatively safe in the relief of ureteric obstruction, including malignancy (Grabstald & McPhee, 1973; Mann et al, 1980, 1983; Soper et al, 1988). Our study supports its effectiveness and low rate of serious complications. The use of bilateral nephrostomy tubes conferred no greater benefit on renal function than the use of a unilateral tube. Thus the low complication rates are further diminished. Local symptoms, for example the presence of pyonephrosis, may dictate the need for bilateral tubes.

Indications for tube insertion are less problematic where there is a possibility of effective therapy for the tumour or a diagnosis has not been reached. This was the case in ten patients (58%). However, for these patients and others where the prognosis is more certain, it is important to assess survival time and quality of life.

Grabstald and McPhee's (1973) definition of a useful life of minimal pain, few complications, full mental faculties and ability to return home for at least two months to participate in family life is a reasonable definition, although these may not be the only considerations for the individual. Our results have shown that 58% of people were able to return home or be cared for in a specialized hospice.

The median overall survival of 18 weeks, and 16 weeks for those with a distant primary, is reasonable by the above definition. Our results are slightly more favourable than the recent study of Keidan et al (1988) whose overall median survival was 13 weeks with only 35% of patients leaving the hospital. Although assessment of the quality of life is subjective, the responses from our questionnaires indicated that in nearly all cases the nephrostomy tubes were well tolerated by patients. At home or in the hospice, very few problems were encountered.

Ureteric stents were subsequently inserted into four patients, selected by the referring oncologist. Since antegrade and retrograde stenting requires either general anaesthesia or further intervention, this was reserved for patients in whom a reasonable life expectancy was envisaged. Where appropriate and technically feasible, this may be the optimal method for long term relief of obstruction (Hepperle et al, 1979).

In conclusion, we have confirmed that percutaneous nephrostomy is effective in improving renal function in malignant ureteric obstruction. The use of bilateral tubes confers no greater benefit to improved renal function than the use of unilateral tubes. Our median survival times and quality of life were acceptable. Intervention in malignant ureteric obstruction should not necessarily be viewed with as much pessimism as in the past. Ultimately, however, the decision to place a nephrostomy tube lies with the physician, family and above all the patient.

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Ultrasonic evaluation of gallbladder function prior to non-surgical treatment of gallstones

By J. S. Beswick, BSc, MBChB, P. M. Hughes, MRCP, FRCR and *D. F. Martin, MRCP, FRCR

Department of Diagnostic Radiology, Withington Hospital, Nell Lane, Withington, Manchester M20 8LR, UK

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Keywords: Gallbladder, Ultrasound, Gallstones

Abstract. A comparative analysis of ultrasonic and oral cholecystographic assessment of gallbladder function in symptomatic patients with cholelithiasis is presented. Ultrasonic evaluation demonstrated non-contractile gallbladders in all but one patient with non-opacification during oral cholecystography, whereas all those opacifying on oral cholecystography contracted on ultrasonography. Both techniques showed similar abilities to quantify the size and number of biliary calculi within the limits necessary to determine suitability for treatment. Although computed tomography remains necessary to quantify gallstone density prior to non-surgical treatment, ultrasonography is a safe, acceptable, cheap and preferable alternative to oral cholecystography in assessing gallbladder function.

The non-surgical treatment of gallstones using oral dissolution therapy (ODT), direct chemical solvents or extracorporeal shockwave lithotripsy (ESWL) requires a functioning gallbladder (Bellamy & Hicks, 1988; Simeone et al, 1989; Torres & Nelson, 1989). Oral cholecystography (OCG) assesses concentrating ability, cystic duct patency and contractility following a fatty meal, while preliminary films differentiate calcified from non-calcified gallstones, but the use of contrast medium and ionizing radiation should preclude its repeated use.

Ultrasonography represents a safe, simple and direct method of assessing gallbladder contractility, inferring cystic duct patency, and can be used to count the number of gallstones in the gallbladder and to assess their size and mobility.

This study was designed to compare the ultrasonic and oral cholecystographic assessment of gallbladder function in symptomatic patients with cholelithiasis.

Method

After exclusions 34 consecutive symptomatic patients with gallstones being considered for non-surgical treatment were evaluated ultrasonographically, 25 also having OCG. Two patients were excluded from the study, one because of hospital admission for abdominal pain and vomiting following ingestion of the Biloptin capsules, the other due to non-visualization of the gallbladder ultrasonographically due to obesity and bowel gas.

Using a 3.5 MHz realtime sector scanner, the common bile duct diameter was measured to exclude obstruction. Imaging was performed in longitudinal and transverse planes with the patient in the right anterior oblique (RAO) position. The volume of the gallbladder was calculated using the ellipsoid method (volume = $(\pi/6) \times \text{length} \times \text{diameter} \times \text{height}$), the formula having been programmed into the computer software (Dodds et al, 1985). The number and size of gallstones within the gallbladder were also recorded.

The resting gallbladder volume was measured following an overnight fast and further volume measurements were taken at 15, 30, 45 and 60 min after a fatty meal, which consisted of Calogen (long-chain triglyceride emulsion, Scientific Hospital Supplies Ltd, Liverpool, UK) fruit flavouring and water providing 30 g fat in a total volume of 250 ml. The mean of two volume estimations was recorded. The maximum ejection fraction was calculated as the difference between the minimum volume achieved and the fasting volume expressed as a percentage of the fasting volume.

This technique has been validated using 42 normal volunteers, the intra-observer error being 7.2% and inter-observer error 9.8% (Beswick et al, 1989).

Oral cholecystography was performed concurrently in 25 cases, the control film having been taken the day before and 6 or 12 Biloptin capsules ingested that night. Erect and prone films were taken before the fatty meal and a prone oblique film was taken 30–45 min later.

Results

Thirty-two patients (18 males and 14 females) were studied, mean age 56.3 years (range 27–77 years). Of these, 12 (37.5%) showed no contraction on ultrasonography, their mean age being 56.2 years (range 37–75 years) and the mean fasting gallbladder volume being 32.5 ± 38.3 ml varying from a small 1.6 ml gallbladder full of tiny stones to a large 113.0 ml gallbladder containing five or six small non-calcified stones. Ten of these had OCG, none of which showed opacification (Table I).

Of the 20 patients (62.5%) who showed contraction on ultrasonography, 15 had OCG, all but one of these

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*Author for correspondence.

Table I. Opacification on oral cholecystography and contraction on ultrasound

Ultrasound	Oral cholecystography	
	Opacification	No opacification
Contraction	14	1
No contraction	0	10

Table II. Comparison of gallbladder characteristics of volunteers and patients with a functioning gallbladder containing gallstones

	Volunteers	Patients
Number	43	20
Age (years)	32 (20–65)	56 (27–77)
Fasting volume (ml) (±2 SD)	19.2±10.4	34.8±19.1
Mean ejection fraction (%) (±2 SD)	63.1±18.4	58.3±19.5
Emptying rate 0–15 min (ml/min)		
Fasting volume 0–15 ml	0.17	0.35
15–30 ml	0.70	0.74
>30 ml	1.33	1.16
Mean rate	0.60	0.84

Table III. Criteria relating number and size of stones to suitability for NST

	Number	Size
ODT	No limit	<2 cm
ESWL	<3	<3 cm
MTBE	No limit	No limit

showing opacification. This patient had a fasting gallbladder volume of 36.7 ml and an ejection fraction of 15% 45 min after the fatty meal. The mean age of this group was 56.3 years (range 27–77 years) with a mean fasting volume of 34.8±19.1 ml (range 10.4–83.1 ml). The mean maximum ejection fraction was 58.3±19.5% with a mean emptying rate of 0.84 ml/min over the first 15 min. These results are shown in Table II compared with the results of our normal volunteers.

No correlation was found between age and fasting volume or ejection fraction, nor between fasting volume and ejection fraction for either group.

The number of stones detected by the two methods and their size were comparable. Those patients with a non-functioning gallbladder on OCG were not included in this analysis as we wished to compare the two techniques for use with non-surgical treatment of stones, for which a functioning gallbladder is essential.

Discussion

The trend towards non-surgical treatment (NST) of gallstones has been accompanied by increased demand for OCG, because non-opacification or minimal contractility of the gallbladder represents a contraindication to ODT and ESWL. Conversely, it has been suggested that treatment with the direct contact solvent methyl *tert*-butyl ether (MTBE) is best performed when the cystic duct is occluded to minimize the toxic effects of MTBE in the duodenum (Simeone et al, 1989). While opacification of the gallbladder during OCG is a good indicator of cystic duct patency, lack of patient compliance or gastrointestinal disorders may cause failure of gallbladder opacification and lead either to exclusion from NST or a repeat examination. Ultrasonography is a safe, cheap and reliable method of assessing gallbladder volume (Beswick et al, 1989) and we have therefore compared OCG and ultrasonic parameters of function in response to a standard fatty meal in all patients referred with symptomatic gallbladder calculi being considered for NST. The abilities of OCG and ultrasonography to determine the size and number of stones were compared as these factors can also determine suitability for specific non-surgical treatments (Simeone et al, 1989).

The effect of age on gallbladder emptying has been studied in the past (Boyden & Grantham, 1926) when it was found that, once adulthood had been reached, the rate of gallbladder emptying remained constant. In our studies, no significant correlation has been found between age and fasting volume or ejection fraction for either the volunteers or the patients with functioning gallbladders, which is in accordance with the previous results. Thus, the difference in the mean age of the volunteers and the patients in our study is unlikely to be relevant.

Of interest is the apparent difference between the mean fasting volumes of the two groups in our studies (volunteers 19.2±10.4 ml; patients 34.8±19.1 ml). This cannot be explained by differences in age. Previous studies have shown no difference in volumes (Maudgal et al, 1980) and it may be that the mean fasting volume of our patients is artificially high owing to one or two unusually large gallbladders. Certainly, when the groups are divided according to fasted volume, the emptying rates of the patients are the same as the volunteers, suggesting that there is no real difference between them. The mean emptying rate for the patients is high (0.84 ml/min) but this merely reflects the large mean fasting volume. Maugdal et al (1980) found an increased post-prandial emptying of the gallbladder in patients with cholesterol gallstones, but other authors have found the opposite (Bobba et al, 1984; Pomeranz & Shaffer, 1985). Our study also failed to confirm this.

Bellamy and Hicks (1988) concluded that ultrasonography and a plain radiograph are sufficient for assessment of gallbladder function before dissolution therapy. They measured cross-sectional areas of gallbladders using a circumference tracing facility and calculated the percentage change following a fatty meal. We used the ellipsoid method to calculate gallbladder volume and hence ejection fraction. We noted that the cross-sections of the gallbladder taken at right-angles to the long axis were not necessarily perfectly round, showing the importance of imaging and measuring in three dimensions. This may account, at least in part, for our failure to find an overlap in the ejection fractions of our non-opacifying group (range 0 to 15.0%, mean 1.2%) with our opacifying group (range 30.8 to 86.8%, mean 58.3%) whereas Bellamy and Hicks (1988) demonstrated a marked overlap (non-opacifying range 21% to −25.5%, mean 1.1%: opacifying range −13.4% to −76%, mean 45.5%). They also showed a wide range in the ejection fractions of the non-opacifying group which may be attributable to measuring in only two dimensions.

Ultrasonography objectively quantified the ejection fraction of the gallbladder in response to the fatty meal in all patients, the intra- and inter-observer errors being under 10% (Dodds et al, 1985; Beswick et al, 1989). OCG provides a more subjective analysis of function, ejection fractions being calculated only after complex calculation accounting for magnification. Ultrasonically non-contractile gallbladders all failed to opacify, a further non-opacified gallbladder showing a low ejection fraction (15%), while the ejection fraction in the remainder of the group was much higher (58%). It is hoped that a prospective analysis relating outcome of NST to the ejection fraction will further improve patient selection for such management. A standardized fatty meal is desirable to produce comparable results on repeat examination. A questionnaire given to normal volunteers in our initial study demonstrated a favourable response in terms of compliance and acceptability for ultrasonography (Hughes & Martin, 1989). However, the limitation of the technique, because of obesity and bowel gas when the gallbladder may be impossible to image, should be borne in mind.

Simeone et al (1989) have suggested a continued need for OCG to quantify the number and size of stones in determining suitability for non-surgical treatments, claiming ultrasonography to be inferior (Table III). Although a certain degree of leeway exists, the size and number appear most important when small numbers of stones (less than five) are being considered for NST, particularly for ODT and ESWL. Both OCG and ultrasonography were equally effective in determining the size and number of less than five stones. Far field acoustic shadowing in assessment of stone size can usually be overcome by positional changes. With more than five stones in the gallbladder it becomes less critical to quantify and assess size particularly when considering ESWL where numerous stones are a contraindication for treatment. Ultrasonography cannot determine calcification and, as this may contraindicate NST, plain films or perhaps computed tomography remain necessary.

In conclusion, we feel that OCG is unnecessary prior to NST for gallstones. Patients should have ultrasonographic assessment of function using a standard fatty meal, gallbladder volume measured before and between 45 and 60 min after fat with either computed tomography or plain films to assess calcification of gallstones.

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Imaging of neonatal pulmonary sequestration including Doppler ultrasound

By *L. M. Smart, FRCR and G. M. A. Hendry, FRCR

X-Ray Department, Royal Hospital for Sick Children, Sciennes Road, Edinburgh, UK

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Keywords: Neonatal pulmonary sequestration, Doppler ultrasound

Abstract. Seven cases of neonatal pulmonary sequestration are reviewed which illustrate the varied clinical presentations and radiological findings. In four patients, real time ultrasound scanning was used to image the chest and the features are described. In three cases, the systemic supplying artery was demonstrated by duplex Doppler scanning and further invasive investigations were avoided; after a chest radiograph, this should be the examination of choice in the investigation of a neonate with a possible pulmonary sequestration.

Pulmonary sequestration presenting in the neonatal period is relatively uncommon comprising 13–25% of all cases (De Paraedes et al, 1970; Buntain et al, 1977; John et al, 1989). Diagnosis may be delayed because of variable clinical and radiological features (Felson, 1972). We review seven cases of neonatal sequestration which presented to the Royal Hospital for Sick Children, Edinburgh, and illustrate the different presentations of the condition. In the last four cases we describe the ultrasonic appearances, including duplex Doppler scanning which avoided further invasive investigations.

Case reports

Case 1

A 5-week-old girl presented with cough and cyanosis. A chest radiograph showed an opaque right hemithorax with shift of the mediastinum to the right. A barium swallow demonstrated an oesophageal bronchus compatible with a total lung sequestration (Fig. 1). Surgery confirmed these findings and the entire lung was removed.

Case 2

A female infant presented at age 2 weeks with respiratory distress and choking attacks. A chest radiograph showed complete opacification of the right hemithorax and shift of the mediastinum to the right with patchy opacification and increased pulmonary vascularity in the left lung. A contrast swallow revealed the right main bronchus originating from the oesophagus indicating a total sequestration. At surgery the small sequestrated lung was removed. Unfortunately, the child died in the post-operative period.

Case 3

A female infant was born at 37 weeks gestation by spontaneous vaginal delivery (SVD). Mild respiratory distress was noted at birth. Radiography revealed opacification in the left hemithorax suggestive of left lower lobe consolidation (Fig. 2). Unusually, the mediastinum was shifted to the right. Ultrasound showed a solid lesion with a hyperechoic rim suggestive of a sequestration (Fig. 3). A radioiostope ventilation/perfusion lung scan confirmed no ventilation or perfusion to the left lower zone. A barium swallow showed no oesophageal bronchus. A bronchogram was performed which showed all the segmental bronchi to be present but the left lower lobe bronchus displaced superiorly. An aortogram revealed a systemic feeding vessel arising at the T12/L1 level (Fig. 4). Surgery and pathology confirmed an extralobar sequestration.

Case 4

A baby girl born at term by SVD at another hospital suffered immediate acute respiratory distress. A chest radiograph showed an ill defined mixed radio-opaque and radio-

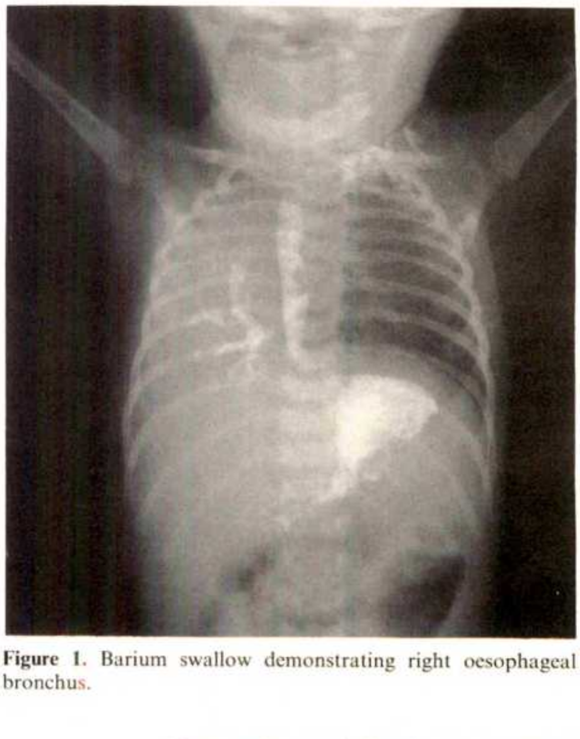

Figure 1. Barium swallow demonstrating right oesophageal bronchus.

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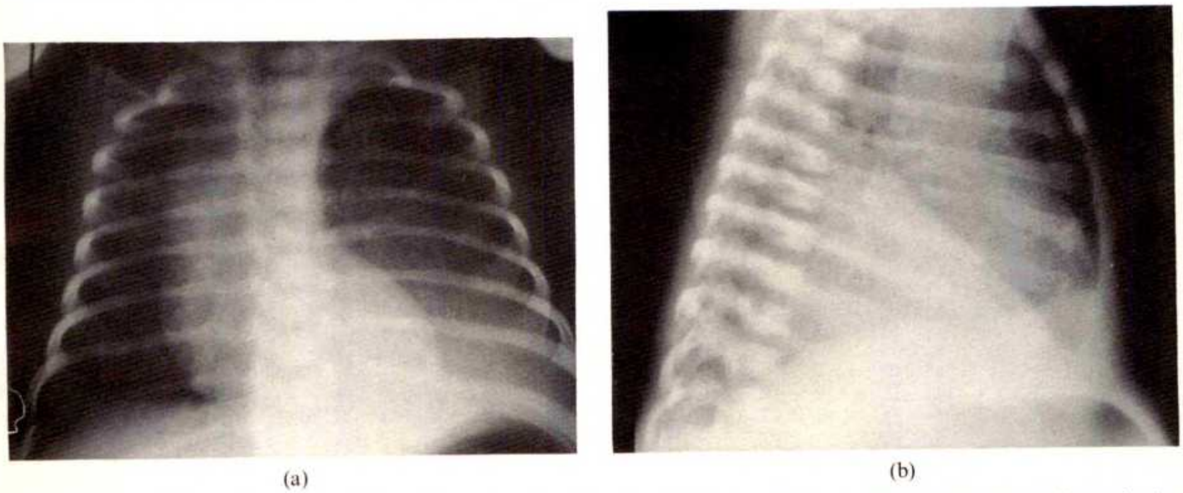
* Current address: X-Ray Department, Royal Infirmary of Edinburgh, Lauriston Place, Edinburgh, UK.



(a) (b)

Figure 2. Antero-posterior chest radiograph demonstrating left lower lobe opacification. (b) Lateral chest radiograph: the sequestration simulates left lower lobe consolidation.

lucent mass in the left hemithorax causing marked shift of the mediastinum to the right (Fig. 5). This had been interpreted as a pneumothorax and a left chest drain had been inserted with no improvement. On transfer to this hospital emergency surgery was performed because of her poor condition, revealing a large extralobar sequestration. The post-operative radiograph showed a persistent shift of the mediastinum to the right and a radioisotope ventilation/perfusion lung scan confirmed that the remaining right lung was hypoplastic.

Case 5

A boy born by SVD at 35 weeks gestation became floppy and cyanosed 5 minutes after delivery. Radiography showed a

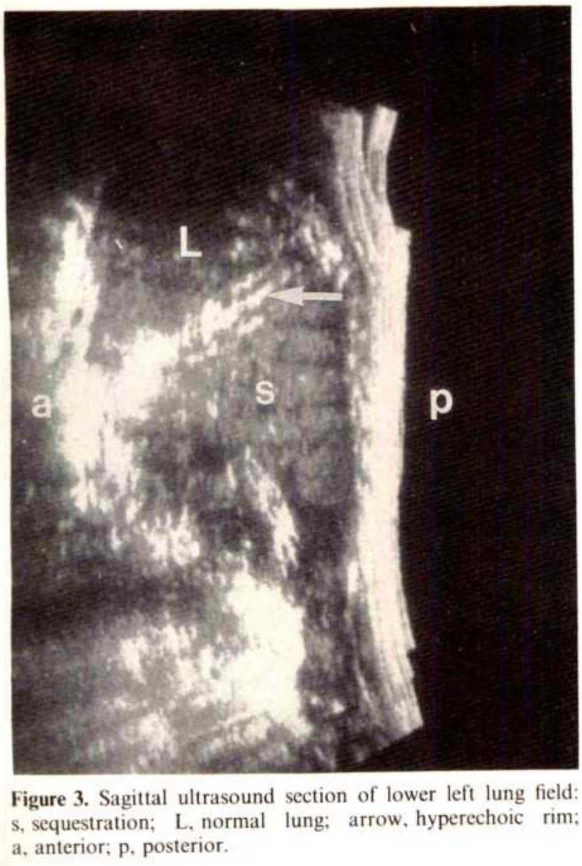


Figure 3. Sagittal ultrasound section of lower left lung field: s, sequestration; L, normal lung; arrow, hyperechoic rim; a, anterior; p, posterior.

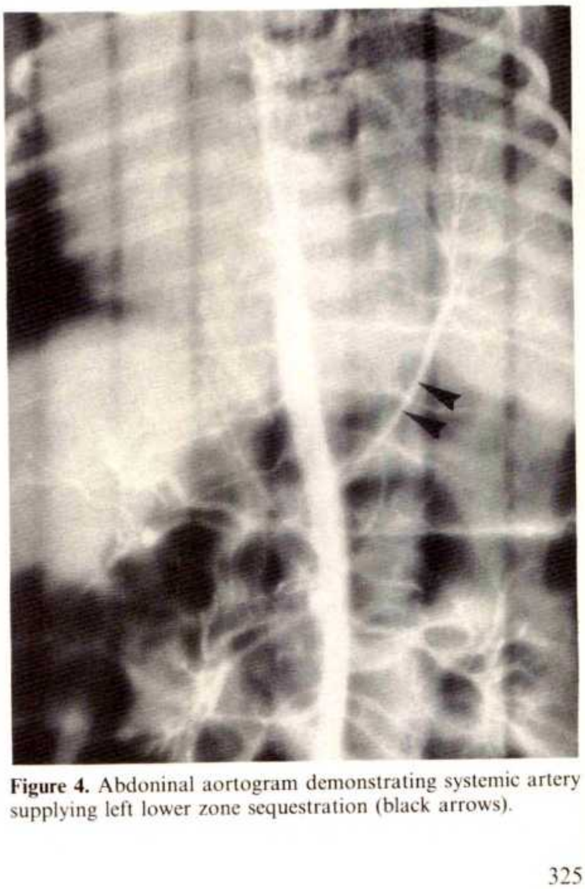


Figure 4. Abdoninal aortogram demonstrating systemic artery supplying left lower zone sequestration (black arrows).

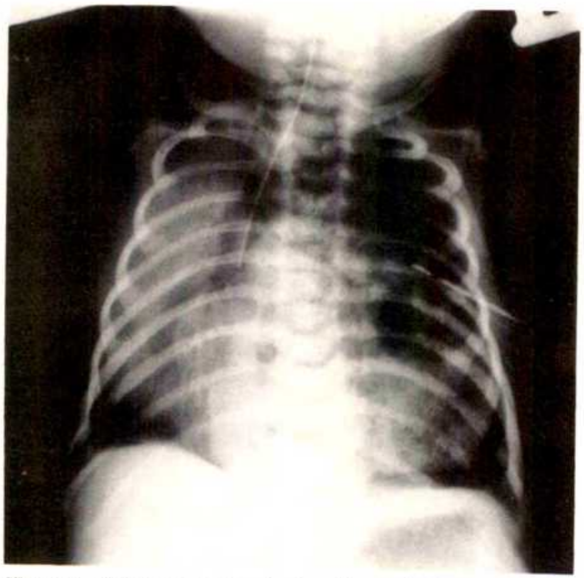


Figure 5. Antero-posterior chest radiograph demonstrating a mixed air-filled cystic and solid mass in the left hemithorax; note presence of pleural drain.

well defined left lower zone opacity lying posteriorly (Fig. 6). The differential diagnosis included sequestration, diaphragmatic hernia or a posterior mediastinal mass. No bowel gas was seen above the diaphragm. Ultrasound examination demonstrated a diaphragmatic hernia containing the left kidney (Fig. 7(a)). A hyperechoic mass was seen lying posteriorly and a supplying vessel visualized. Two-dimensional Doppler scanning with fast Fourier analysis and a frequency time profile demonstrated a systemic arterial configuration (Fig. 7(b)). The spleen was not visible in the abdomen and this mass was thought to represent the spleen. However, surgery revealed an extralobar sequestration attached to the left lower lobe with a supplying vessel from the aorta at the level of the diaphragm. There was a small defect in the posterior part of the diaphragm and the left kidney and adrenal gland had herniated into the chest. The spleen was lying posteriorly in the abdomen. Histological examination confirmed an extralobar sequestration.

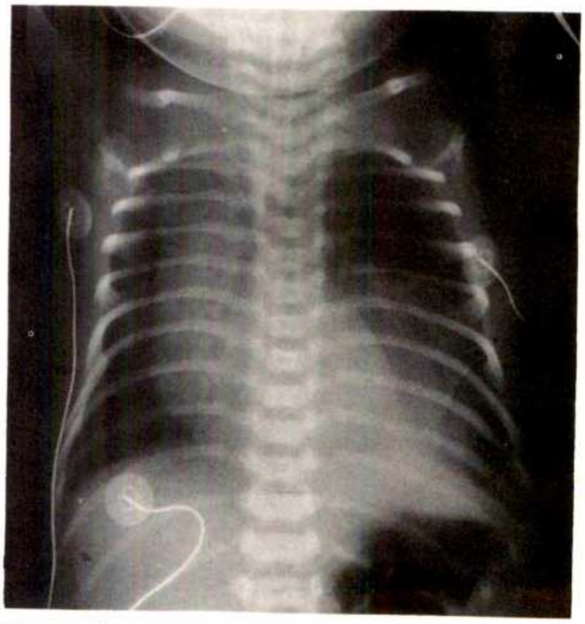
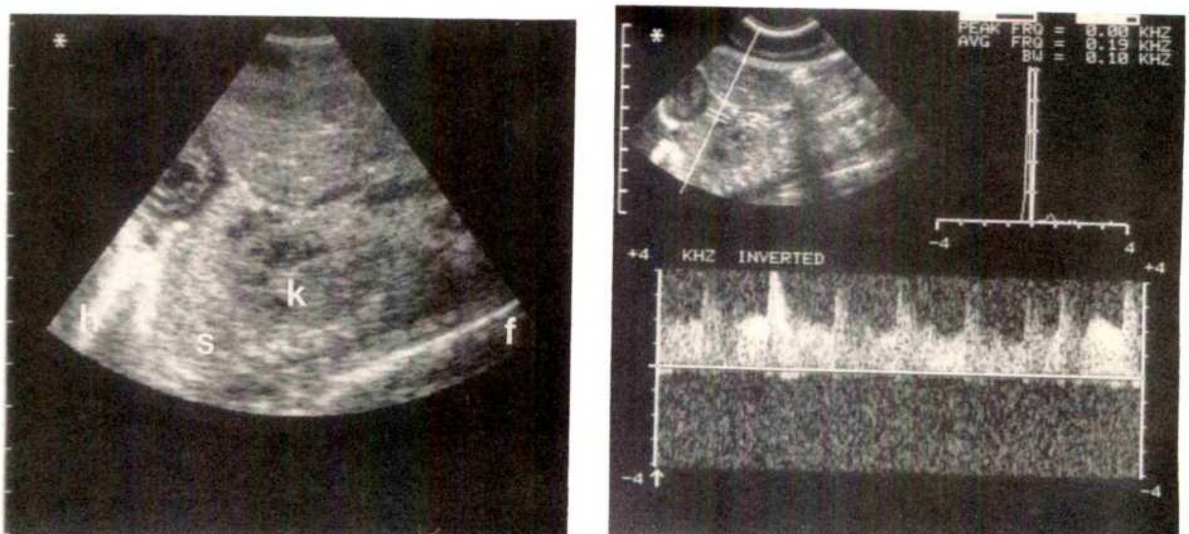


Figure 6. Antero-posterior chest radiograph demonstrating a well defined left lower zone opacity; mediastinal shift to the right is present.



(a)

(b)

Figure 7. Oblique sagittal ultrasound section through the lower left hemithorax: k, kidney, s, sequestration; h, head; f, foot. (b) Doppler recording from the vessel supplying the sequestration, showing a systemic arterial waveform.

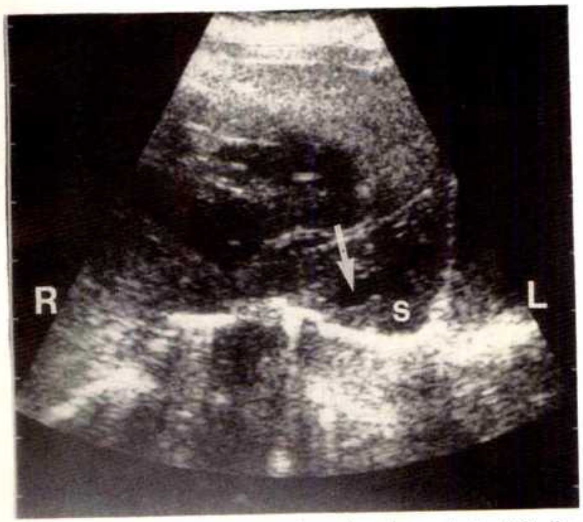


Figure 8. Transverse ultrasound section through the left diaphragmatic area: s, sequestration; arrow, supplying artery; R, right; L, left.

Case 6

A boy born at term by SVD developed jaundice on Day 5. A mass palpable 2 cm below the left costal margin was thought to be an enlarged spleen. An infection screen was negative. A chest radiograph was normal. Ultrasound scanning showed a normal liver and spleen. A triangular echogenic mass in the left subdiaphragmatic area was noted (Fig. 8). This was supplied by a systemic artery arising from the aorta above the coelic axis, confirmed by Doppler analysis, and was thought to be a subdiaphragmatic sequestration. A barium swallow revealed no connection to the gastrointestinal tract. The jaundice resolved. He was asymptomatic and therefore managed conservatively. An ultrasound examination one year later showed no change. He remains well at 18 months old.

Case 7

A boy was born by Caesarean section at term after a failed trial of labour. An antenatal scan at 24 weeks gestation, performed because of a "large for dates" uterus and some abdominal discomfort, showed polyhydramnios and a triangular fluid-filled space in the left hemithorax displacing the mediastinum to the right. The left lung appeared to be compressed by the fluid (Fig. 9). Over the next 6 weeks the fluid-filled space reduced in size and the mediastinum became central. The liquor volume also decreased to normal. After birth he was well. A chest radiograph revealed a soft tissue mass behind the heart in the left hemithorax. An ultrasound examination showed an echogenic mass (Fig. 10) with tubular structures within it on certain sections. The differential diagnosis was extended to include cystic adenomatoid malformation. At 1 month he remained well and a repeat ultrasound showed a homogeneous echogenic mass interposed between the left lung and the hemidiaphragm which appeared intact. A vessel was seen running into the lesion from the upper aorta above the coeliac axis (Fig. 11) and was confirmed as arterial on Doppler scanning, establishing the diagnosis of sequestration. Surgery was performed and this confirmed an extralobar sequestration in the left lower lobe with a supplying vessel from the aorta as predicted by ultrasound.

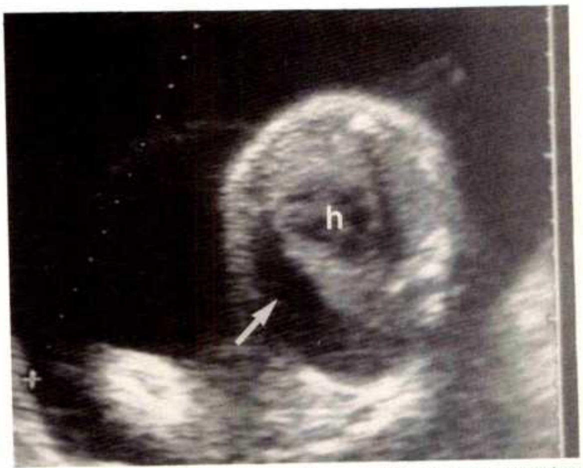


Figure 9. Antenatal transverse ultrasound scan demonstrating left pleural effusion (arrow); h, heart.

Discussion

Pulmonary sequestration is a congenital mass of non-functioning pulmonary tissue with no normal connection with the bronchial tree or pulmonary arteries and which is supplied by a systemic artery from the aorta. It may be intralobar, being encased in the same pleura as the adjacent lung, or extralobar, with a separate pleural covering. Neonatal cases are usually extralobar (De Paraedes et al, 1970; Buntain et al, 1977). A recent review, however, contained a few cases of neonatal intralobar sequestration (John et al, 1989). All our cases were extralobar. There are several theories regarding aetiology but the most favoured is that there is an additional tracheobronchial bud which develops from

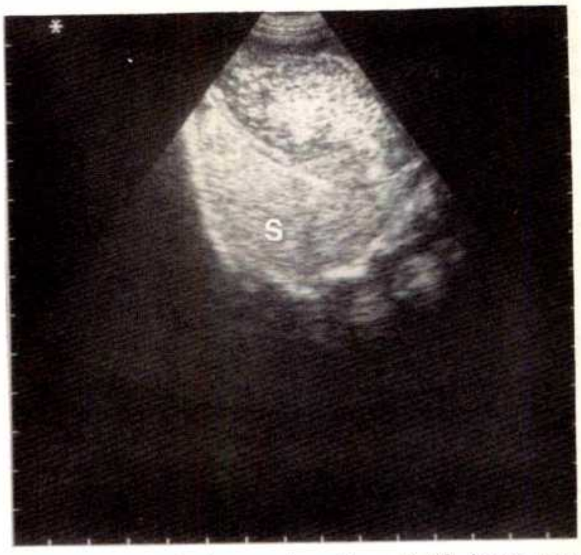


Figure 10. Sagittal ultrasound section of left lower zone demonstrating a meniscus-shaped echogenic appearance of the sequestration (s).

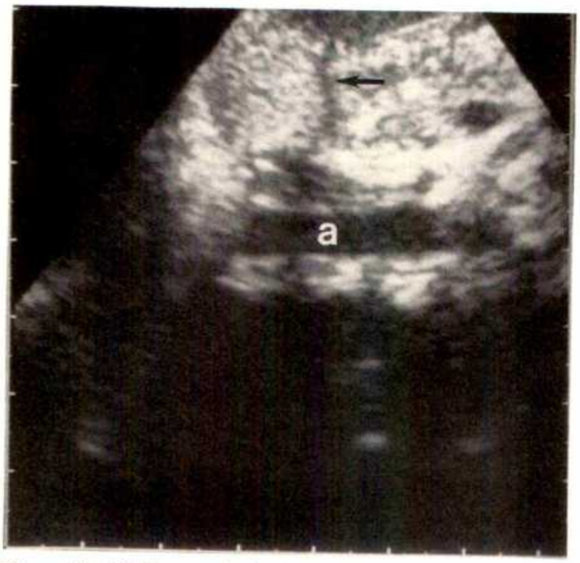


Figure 11. Midline sagittal ultrasound section through the upper abdomen revealing systemic artery (arrow) supplying the sequestration; a, aorta.

the primitive foregut and becomes the sequestration. The time of budding determines whether it is intralobar or extralobar and it may have a residual connection to the gastrointestinal tract (Gerle et al, 1968). This would then explain the rare connection with the oesophagus or stomach (Heithoff et al, 1976). This occurred in two of our cases, an unusually high proportion.

The majority of our cases (five out of seven) were left sided which is typical but the female predominance is unusual for extralobar sequestration (Carter, 1969). The commonest clinical presentation was with respiratory symptoms in five out of seven, an abdominal mass in one, and in one case the patient was asymptomatic, the diagnosis having been made antenatally. The radiographic findings were of a well defined lower zone opacity in four out of seven, with a differential diagnosis of mediastinal mass, consolidation or diaphragmatic hernia. There was complete opacification of the left hemithorax in two out of seven, with a differential diagnosis of pleural effusion, collapse or hypoplasia. In one case the radiograph was normal where there was a subdiaphragmatic sequestration.

An ipsilateral diaphragmatic hernia may be associated with extralobar sequestration, as in Case 5, in approximately 30% of cases (Felson, 1972). Five per cent of cases may be subdiaphragmatic and present as an abdominal mass, as in Case 6 (Carter, 1969). The differential diagnosis then includes splenic tissue and neurogenic tumours.

Recently, ultrasound has been used to image sequestration. Typical appearances are of a uniformly echogenic mass (Haller et al, 1980; Jaffe et al, 1982) which distinguishes it from a pleural effusion or diaphragmatic hernia. Cases 5–7 show these features and Case 3 also illustrates the occasional occurrence of a thin hyperechoic rim which may distinguish it from collapse or consolidation (Kaude & Laurin, 1984).

Ultrasound may detect a diaphragmatic hernia but, as illustrated in Case 5, it may be difficult to make a firm diagnosis of an associated sequestration. A high index of suspicion should be maintained.

There have been several reports of identification of pulmonary sequestration with antenatal sonography (Romero et al, 1982; Joupila et al, 1983; Weiner et al, 1986). These cases have been associated with non-immune hydrops fetalis, all having pleural effusions, unilateral in one case, and maternal polyhydramnios. In some cases there was also generalized fetal oedema and ascites. The sequestration was identified as an echogenic mass separate from the lung. This is thought to be due to hydrops obstruction of venous return to the heart, which may explain the findings in Case 7, although the sequestration was not identified. Pulmonary sequestration should be considered as a cause of non-immune fetal hydrops and included in the differential diagnosis of an intrathoracic mass identified during antenatal scanning.

Although these features are highly suggestive of sequestration, the diagnosis is confirmed if a systemic feeding vessel is demonstrated. In the past this needed angiography, but recently there have been reports of ultrasonic demonstration of the supplying vessel in both real time (Kaude & Laurin, 1984; Cazaban et al, 1987) and by duplex Doppler scanning (Zimmerman et al, 1986; Andres et al, 1989). In Cases 5–7, we demonstrated a supplying systemic vessel arising from the aorta using duplex Doppler scanning. These patients did not have angiography and the ultrasonic findings were confirmed at operation.

There have been recent reports of demonstration of the supplying vessel using dynamic computed tomography scanning (Miller et al, 1982). However, not only is this time consuming, but it also involves radiation and requires sedation and intravenous contrast with their inherent risks. Ultrasound is widely available, simple to perform and non-invasive. We believe that, after a chest radiograph, duplex Doppler ultrasound should be the investigation of choice in a neonate with possible sequestration. It is our opinion that the diagnosis can be made if the systemic supplying vessel is demonstrated and there is then no requirement for further invasive procedures in such cases. We do not believe that angiography is mandatory in all cases as has been previously suggested (John et al, 1989). In addition, if there is a history of respiratory distress or choking episodes, a contrast swallow should be performed to look for a communication with the gastrointestinal tract.

Acknowledgments

We are grateful to Dr B. B. Muir, Consultant Radiologist at the Simpson Memorial Maternity Pavilion, who performed the antenatal ultrasound in Case 7, for Fig. 9.

We should like to thank Miss Susan Duff for her help with organization and typing of this article.

and this was also correct 85% of the time. In the normal patients included in the study a definite diagnosis was reached on chest radiography in 45% and this was correct in 76% of cases. This contrasts with a definite diagnosis being reached on HRCT in 100%, this being correct 96% of the time. This underlines the role of HRCT in confirming or refuting the presence of abnormality when the chest radiograph is questionably abnormal.

Computed tomography of the thorax in chronic berylliosis

K. M. Harris, H. Adams and *K. McConnochie
*Departments of Radiology and *Chest Medicine, Llandough Hospital, Penarth, South Glamorgan CF6 1XX, UK*

Prolonged inhalation of beryllium dust induces a chronic granulomatous reaction similar to sarcoidosis and often progressing to pulmonary fibrosis The plain radiographic appearances are well known but the computed tomography (CT) appearances have not previously been described. Computed tomography of the thorax, incorporating narrow collimation sections, was performed in five male patients with proven chronic berylliosis. A standard posteroanterior radiograph was obtained for comparison. The chest radiograph revealed pulmonary nodularity in four cases. This was diffuse in two cases and predominantly basal in two cases. In the fifth case the main feature was upper lobe fibrosis. Computed tomography confirmed the interstitial changes seen on plain films. In the two patients with diffuse nodularity on chest radiography, this was the major CT feature. In the two cases with basal chest radiography changes, a honeycomb appearance was evident with associated sub-pleural cyst formation in one. In the fifth case, upper lobe fibrosis was confirmed. Previously undetected mediastinal lymphadenopathy was demonstrated in one patient with borderline adenopathy in a second. The CT appearances in chronic berylliosis are non-specific but the pattern and the extent of the disease is well demonstrated. Computed tomography may also reveal previously unsuspected lymphadenopathy.

The role of computed tomography in the early diagnosis of invasive pulmonary aspergillosis

C. M. Owens, L. A. Berger, *P. A. Veys, [+]K. Wong,
[+]R. K. Walesby, *A. V. Hoffbrand and *H. G. Prentice
*Departments of Radiology, *Haematology and [+]Cardiothoracic Surgery, The Royal Free Hospital, London NW3 2QG, UK*

Invasive pulmonary aspergillosis (IPA) is a major cause of mortality in neutropenic patients. One of the more recently defined yet common forms of IPA is the apparent formation of a mycetoma in previously normal lung tissue; this differs histologically from the classical mycetoma, and has been given the name mycotic lung sequestrum (MLS). The development of MLS has been associated with a high incidence of fatal haemoptysis, often occurring within one week of diagnosis, which can only be avoided by early surgical removal of the lesion. This study of the clinical presentation of MLS in 14 consecutive patients who were receiving chemotherapy for haematological malignancies at the Royal Free Hospital, shows that the radiological features of MLS have provided the earliest and most accurate guide to diagnosis, enabling prompt surgical resection of the MLS. In particular, computed tomography (CT) was the most effective means of establishing and substantiating the early diagnosis of invasive fungal disease, at a time when plain films were non-specific and fungal cultures were negative. Specific abnormalities included the presence of the "halo"and "air crescent" signs. Consequently, we now advocate the early use of high resolution whole lung CT, both to confirm the clinical diagnosis, and to assess the amenability to prompt surgical resection. This policy has led to the successful resolution of MLS in almost all of the cases studied.

An anatomical and functional correlation of disease activity in fibrosing alveolitis: high resolution computed tomography and ^{99}Tc^{m} scanning

D. M. Hansell, A. M. Wells, C. M. Black, R. Lawrence and R. M. du Bois
Department of Radiology, Royal Brompton and National Heart Hospital, London SW3 6HP, UK

Patients with a cellular lung biopsy in fibrosing alveolitis have a better prognosis and response to treatment than those with a fibrotic appearance; however, non-invasive means of predicting disease activity are largely unreliable. We have demonstrated a strong correlation between fibrotic histology and predominantly reticular abnormalities on high resolution computed tomography (HRCT). Enhanced clearance of inhaled ^{99}Tc^{m} DTPA reflects increased lung epithelial permeability and has been used as a marker of inflammation in several lung disorders. To determine whether the extent and grading of HRCT changes correlate with DTPA abnormalities, we have evaluated the CT scans of 50 patients with systemic sclerosis who have undergone concurrent DTPA scanning. The volume of involved lung was measured by subjective assessment of five interspaced sections, including a weighting factor to allow for volume differences between slices. Whole lung HRCT appearances were graded on a five point scale, from increased parenchymal opacification alone through to reticular abnormalities alone. In the 25 patients with a larger volume of involved lung (greater than 14%), there was an increased frequency of enhanced DTPA clearance (84% versus 36%, $p<0.001$). Enhanced DTPA clearance did not correlate with HRCT grading of parenchymal opacification and a reticular

10.45 – 12.00

Imaging and the Chest

Clarence Room

High resolution computed tomography of the lung: technical factors and clinical indications

A. G. Wilson
Department of Diagnostic Radiology, St George's Hospital, Blackshaw Road, London SW17 0QT, UK

Recent technical developments have allowed greatly improved spatial resolution in computed tomography (CT) of the lung. Such high resolution CT (HRCT) has found wide application in the study of diffuse lung disease. High resolution CT uses thin collimation (1.5 mm), short exposure times, targeted image reconstruction and high resolution algorithms. Exposure factors are increased to typically 170 mA and 140 kV to improve the signal to noise ratio. Because of dose and time constraints, a limited number of scans (4–6) is obtained in a typical HRCT examination, giving a total absorbed dose that is 3–5% of conventional full chest CT. High resolution CT images display fine lung structure, in particular that of the secondary pulmonary lobule. An understanding of this fine anatomy is important in interpreting HRCT images. Normal anatomy and HRTC signs of disease are illustrated. The place of HRCT in the investigation of diffuse lung disease is by no means established. Current applications include the detection of suspected interstitial disease, characterization of interstitial disease, assessment of pneumoconioses, identification of biopsy sites, monitoring disease extent, activity and response to treatment, and the diagnosis of bronchiectasis. These indications are critically assessed.

High resolution computed tomography in pulmonary sarcoidosis: the significance of peribronchial disease

P. M. Taylor, *S. E. Church and *C. H. Hardy
*Departments of Diagnostic Radiology and *Thoracic Medicine, University of Manchester, Manchester M13 9PT, UK*

Several studies have demonstrated the variability of radiological findings in high resolution computed tomography (CT) of pulmonary sarcoidosis. When conventional scoring systems based on the ILO classification are applied, there is poor correlation with pulmonary functional abnormalities. Although the majority of patients show a restrictive pulmonary deficit, a substantial minority will have evidence of airflow obstruction. Bronchographic studies have demonstrated the presence of bronchial strictures in patients with sarcoidosis and airflow obstruction. The aim of this study was to determine whether the presence of peribronchial disease demonstrated on CT indicated a greater incidence of airflow obstruction. Twenty-five patients (16 female, nine male) with known sarcoidosis were studied. High resolution CT was performed using an IGE 9800 system and conventional spirometric testing was carried out within 1 week of the examination. All the computed tomograms were reviewed by a single observer, blind to the clinical and physiological findings, and nine patients with peribronchial disease were identified. No bronchial strictures were identified from CT. This group had significantly lower FEV1/FVC ratios than those without peribronchial disease. None of these patients showed reversibility to bronchodilators. These findings suggest that CT may be of value in the identification of patients with airflow obstruction in sarcoidosis.

Accuracy of high resolution computed tomography versus chest radiography in chronic diffuse infiltrative lung disease

S. Padley, D. M. Hansell, C. D. R. Flower and P. Jennings
Department of Radiology, Royal Brompton Hospital, Fulham, London SW3, UK

The sensitivity of high resolution computed tomography (HRCT) in detecting subtle diffuse infiltrative lung disease (DILD) is now well established. It is increasingly recognized that a specific diagnosis of DILD can be achieved with HRCT; the purpose of this study was to establish the frequency with which a confident diagnosis could be reached on HRCT compared with chest radiography. A study of 100 patients with a definite and specific diagnosis of chronic DILD was undertaken. The case mix included a wide variety of diseases and an unspecified number of normal patients. Two observers viewed the CT and chest radiographs on separate occasions and recorded three differential diagnoses. On the diagnosis thought most likely a score of the degree of certainty was given. Overall, a definite diagnosis was reached more often for HRCT then for chest radiography. Diagnoses made on HRCT were more frequently correct than diagnoses made on chest radiography. A definite diagnosis was reached on chest radiography in 49% of patients and this was correct 85% of the time. A definate diagnosis was reached on HRCT in 55% of patients and abnormal enhancement were also detected in the rectal wall following pelvic radiotherapy. Pelvic recurrence of tumour can usually be separated from post-operative fibrosis on the basis of morphology and signal intensity, but exceptions can occur. Previous pelvic radiotherapy may induce visceral changes mimicking tumour recurrence.

Notes

The role of lymphography in comparison with computed tomography scanning in the management of carcinoma of the cervix

I. Fernando, E. Moskovic, I. Fryatt, J. Glaholm and
P. R. Blake
Department of Radiotherapy and Diagnostic Radiology, Royal Marsden Hospital, Fulham Road, London SW3 6JJ, UK

In order to evaluate the continuing role of lymphography in addition to computed tomography (CT) scanning in the management of carcinoma of the cervix, it was decided to analyse retrospectively 104 cases treated by radiotherapy at the Royal Marsden Hospital between 1984 and 1990. When assessing lymphatic involvement using these two modalities, patients fell into three categories: (1) patients with positive nodes on lymphogram (positive LMG) and positive CT scans (positive CT); (2) positive lymphograms (positive LMG) but negative nodes on CT scanning (negative CT); (3) those with no abnormality on either scan (LMG negative and negative CT). In this study there were no patients who had positive nodes on CT scanning in whom there was no abnormality on lymphography. Our results show that 16 out of 104 patients were LMG positive and CT positive, 15 out of 104 were LMG positive and CT negative, and 73 out of 104 were LMG negative and CT negative. The presence of involved nodes detected only by lymphography significantly altered the subsequent management in five out of six patients with Stage IB disease. They were considered for Wertheim's hysterectomy but instead received irradiation and hence avoided unnecessary surgery. Any such patients could also be considered for the adjuvant chemotherapy studies. Survival analysis on these three different groups showed that patients in group 2 did as badly as those in group 1. Both groups did significantly worse than those in group 3. This appeared to be independent of T stage. We conclude that lymphography still has a role to play in early stage carcinoma of the cervix.

Magnetic resonance imaging and immunoscintigraphy using ^{111}In labelled OC125 in the diagnosis of suspected primary and recurrent ovarian carcinoma

R. W. Kerslake, *I. Symonds, +A. C. Perkins, *† I. V. Scott, M. L. Wastie, *F. M. Symonds and B. S. Worthington
*Departments of Radiology, *Medical Physics and +Obstetrics and Gynaecology, University Hospital, Nottingham NG7 2UH and †Derby City Hospital, Derby DE3 3NE, UK*

Pelvic magnetic resonance imaging (MRI) performed at 0.15 T and radioimmunoscintigraphy (RIS) using the monoclonal antibody OC 125 labelled with ^{111}In have been prospectively compared in the diagnosis of suspected primary (group 1) and recurrent/residual (group 2) ovarian cancer in a total of 41 patients. In group 1, 14 patients were studied and pathological confirmation was obtained in 11. Of those 11, MRI achieved a sensitivity of 40% and specificity of 83% for the diagnosis of ovarian malignancy, compared with 80% and 33% respectively for RIS. Although MRI was not capable of distinguishing stage 1 ovarian carcinoma from benign ovarian tumours, the appearances accurately reflected the gross morphology of the lesions and in one case a diagnosis of uterine enlargement due to multiple leiomyomas rather than of ovarian cancer was correctly made. Twenty-seven patients were studied in group 2, with surgical correlation in 23 cases. The sensitivity of MRI was 88% and specificity 33%, compared with 76% and 67% respectively for RIS. The predictive value of a positive result was 79% for MRI and 87% for RIS with a negative predictive value of 50% for both techniques. Both methods were limited in the detection of very small-volume recurrences. The potential role of these techniques in relation to surgical evaluation is discussed.

Magnetic resonance imaging findings in recurrent pelvic tumour

J. M. Hawnaur, R. J. Johnson, J. P. R. Jenkins and
I. Isherwood
Department of Diagnostic Radiology, University of Manchester, Manchester M13 9PT, UK

The aim of the study was to assess the ability of magnetic resonance imaging (MRI) to demonstrate recurrent pelvic tumour and to differentiate such recurrence from post-treatment changes. Fifty-four patients (32 female, 22 male, aged 17–75 years) with recurrent pelvic tumour suspected clinically or as a result of abnormal post-treatment MR scans were reviewed. Patients had undergone surgery, radiotherapy or chemotherapy for tumours of the female reproductive tract (28), bladder (14), rectum (nine) or musculoskeletal system (three). Magnetic resonance imaging was performed at 0.26 T using spin echo (SE700–2000/26–120) and partial saturation recovery (PSR500/18) sequences. Images were obtained following intravenous administration of gadolinium-DTPA (Gd-DTPA) in 24 patients. Pelvic recurrence of carcinoma of the cervix or ovary was identified as a soft tissue mass with abnormal signal intensity (long T2) end enhancement on T1-weighted images after Gd-DTPA. Local cervical recurrence could not be differentiated from radiotherapy change. Similarly, small recurrent bladder carcinomas could not be differentiated reliably from the mural thickening, high signal intensity and enhancement post-Gd-DTPA observed after radiotherapy. In rectal carcinoma, established post-operative fibrosis had a low signal on both T1- and T2-weighted sequences but was mimicked by scirrhous tumour recurrence. Recurrent rectal tumours enhanced after Gd-DTPA but thickening it difficult to assess recurrent disease. In one patient a diaphragmatic prosthesis was required which resulted in a distinctive CT appearance. The CT appearances before and after surgery are more fully described, and the difficulties of radiological follow-up are discussed.

Computed tomography evaluation of lymph node status in prostate cancer

J. Spencer, *A. Hindley and S. Golding
*Regional Computer Tomography Unit and *Radiotherapy Department, Churchill Hospital, Oxford OX3 7LJ, UK*

The computed tomography (CT) studies performed for staging in 100 consecutive patients with prostate cancer were reviewed retrospectively to assess the incidence and distribution of lymphadenopathy. All had negative bone scans and were candidates for radical radiotherapy. The CT scans of the abdomen and pelvis followed a standard protocol and were supervised by the same radiologist. Sections of 10 mm were obtained at 15 mm intervals from the diaphragm through the abdomen and then contiguously through the pelvis to the pubic symphysis. Oral and rectal contrast media were administered routinely and intravenous contrast medium used selectively where necessary. Eleven patients had lymphadenopathy as judged by established CT criteria, six with pelvic nodal enlargement alone and five with involvement of pelvic and retroperitoneal nodes. No patient had isolated retroperitoneal lymphadenopathy. Comparison of histological grade and "T" stage at CT permits a degree of prediction of the likelihood of lymph node involvement. The lymph node status of these 100 patients compared with that of a further 100 patients with prostate cancer referred for CT for all purposes indicates discrete patterns of nodal involvement. These include a distinct subgroup showing particularly large volume disease. Our findings suggest that CT staging studies of prostate cancer do not need to include the retroperitoneum if there is no lymphadenopathy at or below the aortic bifurcation.

Radiological evaluation of ileal loop diversion following cystectomy for bladder cancer

*J. Noble, D. Kessell and D. Rickards
*Departments of Radiology and *Urology, The Middlesex Hospital, London W1N 8AA, UK*

The concept of the "urothelium" as a continuous membrane lining the urinary tract necessitates careful evaluation of the remaining upper urinary tract in patients undergoing cystectomy for bladder cancer. Intravenous urography (IVU) is conventionally performed in the early post-operative period to ensure satisfactory drainage and at regular intervals following this with the aim of detecting late complications and/or metachronous urothelial carcinoma. However, loopography offers an alternative method of evaluation and we feel it confers several advantages over conventional IVU. We have performed follow-up loopography on 41 patients in the last year who have undergone cystectomy for bladder carcinoma either as part of a regular follow-up regime or as a result of clinical features suggestive of loop complications and/or tumour recurrence. Two patients had radiological evidence of tumour recurrence and in four cases another abnormality was noted. In only one case was an IVU necessary following a failed attempt at loopography due to stenosis at the ileal stoma site. Loopography is a simpler, better tolerated and more accurate method of evaluating ileal loop diversion. The advantages of loopography over IVU will be discussed along with the long-term complications of urinary diversion in these patients.

Radiological and pathological correlation in renal lymphoma

S. A. V. Holmes, M. Scott, T. J. Christmas and W. F. Hendry
Department of Urology, St Bartholomew's Hospital, London EC1A 7BE, UK

Lymphomatous involvement of the kidney is uncommon. Primary renal lymphoma is very rare as the renal parenchyma lacks lymphatic tissue. The distinction, however, between primary lymphoma and metastatic involvement from haematogenous spread or retroperitoneal involvement may not always be possible, and may not alter management. Lesions may be solitary, multiple or bilateral but often present through massive unilateral renal enlargement. This may occur owing to the lack of other attributable symptoms. We present six cases of this condition and review the radiological and pathological correlation in them. The value of computed tomography scanning is emphasized, as it can make a pre-operative diagnosis, facilitate surgical or non-surgical planning and tumour staging. It can also reveal the presence of bilateral lesions, extension of a retroperitoneal mass into the kidney and detect para-aortic lymphadenopathy. Treatment depends on the size, number and location of tumours and the presence of a pre-operative diagnosis. Tumour debulking followed by chemotherapy with or without radiotherapy is the treatment of choice and can result in excellent tumour resolution or cure, depending on the histological typing. Meticulous radiological imaging should facilitate the management of these tumours which have an overall favourable prognosis.

9.00 – 10.15

Imaging in Oncology

Lancaster Room

Magnetic resonance of childhood tumours: present application and future perspectives

M. A. Hall-Craggs
Nuclear Magnetic Resonance Unit, Department of Radiology, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JH, UK

Magnetic resonance (MR) has three important advantages where imaging children with cancer is concerned: (i) ionizing radiation is not used, (ii) extensive preparation, other than adequate sedation, is unnecessary and (iii) high tissue contrast can be generated and vascular anatomy can be shown without the use of intravascular, iodinated contrast agents. Most studies to date (outside the neuraxis) have concentrated on comparing MR with other imaging modalities and have focused on tumours in the abdomen, mediastinum and musculoskeletal system. In general, MR has proved to be at least as good as computed tomography (CT) for assessing the extent of disease, and in many situations is clearly better. However, a number of specific issues remain unresolved and require further study. Tissue characterization by MR has met with limited success (in common with CT and ultrasound) as the appearances of most tumours are non-specific and MR shows tumour calcification infrequently. Reports of MR imaging and spectroscopic assessment of tumour response to therapy have been encouraging and potentially these methods may help timing chemotherapy and surgery. The use of MR contrast agents (such as gadolinium) may further enhance the sensitivity and selectivity of this powerful technique.

Staging of oesophageal carcinoma: magnetic resonance imaging compared with computed tomography

D. Glew, P. Goddard, *D. Alderson and J. Virjee
*Departments of Radiodiagnosis and *Surgery, Bristol Royal Infirmary, Bristol BS2 8HW, UK*

Computed tomography (CT) is used in the pre-operative staging of oesophageal carcinoma, but often leaves doubt as to the presence of mediastinal invasion, or involvement of local lymph nodes and the gastro-oesophageal region. Magnetic resonance imaging (MRI), with multiple imaging parameters and planes of image, high image contrast and cardiac gating, has many potential advantages over CT. This study compares independent CT and MRI staging of 17 patients with oesophageal carcinoma. Magnetic resonance imaging was performed on a Picker 0.5 T Vista HP 2055 scanner, and cardiac gated T1-weighted spin–echo images were obtained in sagittal and axial planes, with short-tau inversion recovery (STIR) axial images. The results of the two staging procedures, surgical and histological findings are discussed. The imaging methods produce broadly similar stages but MRI leads to a greater estimate of mediastinal spread, particularly in the involvement of vascular structures. The imaging parameters of the walls of the oesophagus and of mediastinal vessels diminish some of the possible advantages of MRI as does mediastinal oedema. However, as the operative assessment of spread may be an underestimate, it may be difficult to be certain which estimate of spread is the more accurate.

Computed tomographic appearances following pleuropneumonectomy for malignant mesothelioma

H. Adams, M. S. Bernard and E. G. Butchart
Departments of Radiology and Thoracic Surgery, Llandough Hospital, Penarth, Cardiff CF6 1XX, UK

The prognosis of malignant mesothelioma of the pleura is poor. Although radiotherapy, chemotherapy and subtotal surgical resection may be of value in palliation, they are unlikely to prolong survival. More aggressive treatment involving pleuropneumonectomy and adjuvant chemotherapy may improve the prognosis of patients with early disease. Such treatment is only suitable for selected patients and is only undertaken in a few centres. Patient numbers are consequently small and the results of treatment must be carefully assessed. Although computed tomography (CT) is valuable in monitoring patients with mesothelioma, the appearances following radical surgery can be confusing. We have therefore reviewed the CT appearances of patients who have undergone pleuropneumonectomy at our centre. Computed tomography has been performed on seven male patients following pleuropneumonectomy. Two had died at the time of the review. In six patients the pneumonectomy space was lined by a membrane which enhanced following intravenous contrast medium despite complete resection of the pleura. Pleuropneumonectomy involves complete resection of the ipsilateral diaphragm. In three patients this resulted in marked upward shift of the abdominal viscera into the pneumonectomy space making

Local recurrence following conservative surgery and radiotherapy in early breast cancer: the experience of a regional radiotherapy centre

J. D. Brierley, A. D. Stockdale, N. Bracey and J. Holden
Regional Centre for Radiotherapy and Oncology, St Luke's Hospital, Warren Road, Guildford, Surrey GU1 3NT, UK

Clinical trials have confirmed that local excision and postoperative radiotherapy is effective treatment for early breast cancer. Studies have concentrated on meticulous surgical technique and daily radiotherapy with small fractions. Since 1974 at the Regional Radiotherapy Centre Guildford, a standard of regime of 48 – 49.5 Gy megavoltage irradiation in 15 fractions in 6 weeks on cobalt 60 has been used following wide local excision of operable breast cancer. From the records of the Thames Cancer Registry we have identified and reviewed 364 patients referred for postoperative radiotherapy following local excision between 1st January 1980 and 31st December 1984 by 22 consultant surgeons from seven district hospitals. Local recurrence has occurred in 29 cases (8%) and five patients have relapsed in the axilla alone. In total there were 34 local regional relapses (9.3%). Our results are clearly comparable with published data from other centres. Data will be presented showing the effect of age, T and N stage, completeness of excision, presence of DCIS, radiotherapy boost and adjuvant treatment on local recurrence.

A simple asymmetric field matching technique for intact breast irradiation

A. J. Moloney, G. R. Plant, D. A. L. Morgan and K. B. Slater
Department of Clinical Oncology, Nottingham General Hospital, Nottingham NG1 6HA, UK

In 1984 a linear accelerator was installed in this department which possessed the facility for independent movement of all collimators, enabling treatment fields to be generated that were asymmetrical with respect to the central axis. This immediately resulted in an ability to improve our tangential technique for breast cancer treatment. The asymmetric jaws enable the lower (below central axis) part of the beam to be blocked off, reducing dose to the lung. Previously, using the same setting-up points, we had to offset the angle of the fields and lower the treatment couch to achieve similar matching of the lower borders – a much more cumbersome technique. Although this provided an easy solution for two-beam treatments, it did not solve the problem of matching the tangential to supraclavicular/axillary fields. To enable a reproducible match of the beams it is necessary that the superior borders of the tangential fields should lie in a single vertical plane to match the anterior field's asymmetric caudal edge. To simplify this problem a "breast bed" has been constructed with a variable tilt for the patient's upper torso. To ensure the reproducibility of the patient position on the couch, adjustable arm and feet supports have been incorporated. This ensures that the angle of the chest wall is horizontal and only a small collimator and couch rotation is required to achieve a vertical and coplanar field match at the superior borders. Four hundred and seventy-three patients have now been treated with this technique which provides a simple and reproducible treatment that, we feel, avoids the problems associated with using two collimators asymmetrically.

Measurement of the mucositic changes in the oral cavity

T. Ljubenov
Department of Radiotherapy, Medical Academy 2nd Base, 1142 Sofia, Bulgaria

To make objective the subjective definitions given by three clinical classifications (WHO, Hickey and van der Schueren), we can use numerical values of the mucositic score α. In order to make the data determined "by the eye" more objective, we can also use the method of potential functions. The dividing signs of points in the measured space are sharply distinguished from one another. The signal U_i which is proportional to the generalized contrast K_{ij} increases to $U_i = U_j + UK_{ij}$, where U is half the distance between the asymptotes of the S-shaped curve. It has been calculated experimentally that for the retina of the eye, $\rho = 0.39$. With $\rho = 0.5$ the formula assumes a more simple appearance:

$$K_{ij} = \frac{L_i - L_j}{L_i + L_j}$$

We compare the subjective and objective data in 10 patients suffering from carcinoma of the epipharynx, and the values of the mucositic score. In the case of a strongly expressed mucositis becoming diffuse, the values of α can reach 10.0.

9.00 – 10.15

Fractionation in Palliative Radiotherapy

Balmoral Room

"T'were best t'were done quickly": a guiding principle for palliative radiotherapy?

T. J. Priestman
Radiotherapy Department, The Royal Hospital,
Wolverhampton WV2 1BT, UK

Palliative treatment accounts for between 40 and 60% of the workload of British radiotherapy departments. In recent years a number of randomized prospective clinical trials have compared different radiotherapy schedules in the treatment of bone metastases, inoperable non-small cell lung cancer and cerebral secondaries. These studies have suggested that shorter dose–fractionation regimens are as effective as longer schedules in relieving symptoms and do not increase morbidity. Short treatment courses have the advantage of reducing the burden on both the patient and departmental resources. Critics of this approach argue that single or short course treatments may not give such long-lasting control of symptoms as longer regimens and may adversely affect overall survival. Others have suggested that defining palliation only in terms of symptomatic relief is unduly limiting the role of radiotherapy and that treatment should be given to those patients who are asymptomatic but known to be at risk of developing problems and that in this situation longer courses of treatment are appropriate. The evidence for and against these various propositions will be discussed.

Conservative surgery and radiation therapy in stages I and II breast carcinoma: local control and cosmetic outcome

A. Roelstraete, M. van Lancker, A. de Schrijver and
G. Storme
Department of Radiotherapy, University Hospital Ghent,
Ghent 9000, Belgium

Between 1980 and 1987, 118 patients with stages I and II breast carcinoma underwent conservative surgery and radiation therapy. Median follow-up from the date of surgery was 48 months. All patients were followed for at least 2 years. Six of the 118 patients developed local recurrence. Half of them occurred in the same quadrant. A Paget's disease was observed in one of the other three cases. Median time to failure was 22 months. Sixty-seven patients were evaluable for cosmetic outcome. All patients received 6900 cGy by external beam (8 MV photons by means of a linear accelerator) to the entire breast. In 67% of the cases an axillary field was administered. The overall cosmetic result was judged by a panel to be excellent or good in 62%, fair in 26% and poor in 12%. Patients themselves found the cosmetic result to be excellent or good in 94%. Breast asymmetry (retraction of the inferior border of the breast ($P = 0.00001$), surface difference between both breasts ($P = 0.000001$), breast induration ($P = 0.005$), retraction of the scar ($P = 0.000001$) and telangiectasia ($P = 0.001$) correlated with the cosmetic score. The type of surgery, the resection volume, axillary irradiation and the use of bolus significantly influenced the cosmetic outcome.

Radioiodine dose response in differentiated thyroid carcinoma

M. E. A. O'Connell, M. A. Flower, C. L. Harmer and
V. R. McCready
Thyroid Unit, The Royal Marsden Hospital, Downs Road,
Sutton, Surrey SM2 5PT, UK

Accurate measurement of the absorbed dose of ^{131}I in thyroid remnants and differentiated metastases is desirable in order to achieve curative treatment whilst avoiding the potential morbidity of excessive therapy. A dual-headed rectilinear scanner with special high-resolution low-sensitivity collimators has been designed to image and quantify therapy levels of ^{131}I. This is now being used together with positron emission tomography to achieve improved accuracy in the estimation of functioning tumour volume, which may differ from the anatomical volume. Dose–response data have been obtained for 31 patients. Following total thyroidectomy and 3 GBq ^{131}I, a mean absorbed dose of 384 Gy achieved complete ablation of thyroid bed remnants in 72% of patients. Patients who had persistent uptake in the thyroid region on subsequent radioiodine scanning received a mean dose of only 69 Gy. Cumulative doses in excess of 150 Gy were found to eradicate cervical nodal metastases following neck dissection. Patients with bone metastases (who generally have a very poor prognosis) received doses of the order of 20 Gy. The dose–response curves explain the varying clinical response to fixed activities of radioiodine and in future will enable precise prescription of radioiodine to achieve tumouricidal doses whilst avoiding the morbidity of excessive therapy.

9.00 – 12.00

Consensus Workshop: Will your Radiology Department be Financially Viable in the Wake of the White Paper Changes?

Norfolk Room

G. de Lacey
Department of Radiology, Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex HA1 3UJ, UK

The workshop will be divided into three 1-hour sections (A,B,C). (A) What is the financial risk to the District Hospital? Is there a particular risk to the Teaching Hospital? (B) The Radiology Department in the Rural Hospital; What risk? Where are the Competitors? (C) The Radiology Department in the Metropolitan Hospital: 'Some will profit, others will go to the wall' – an economic reality, or a practical fiction? In each 1-hour session there will be two to three invited speakers, each giving their view over 10–15 minutes. These presentations to form the basis of 30 minutes of discussion with the audience. Invited speakers include Professor Peter Armstrong, Department of Radiology, St Bartholomew's Hospital; Mr R. Atkinson, Superintendent Radiographer, Norfolk and Norwich Hospital; Dr Michael Brindle, Department of Radiology, Queen Elizabeth Hospital, Kings Lynn; Dr Colin Connolly, Managing Director, ASLAN Medical Consultants & Information Services; Dr Sholum Glouberman, Kings Fund College; London Dr John Hutton, Centre for Health Economics, University of York; and Dr Andrew Porter, William Harvey Hospital, Ashford, Kent.

toms. In 11 patients not initially considered for second opinions but eventually referred, three patients had negative radiology with symptomatic improvement whilst a further six with persisting symptoms showed minor degenerative changes. One asymptomatic patient with Forestiers' hyperostosis was referred because of lack of familiarity with the condition. Six patients with negative radiology and nine with no or improved symptoms were referred for second opinions whilst two patients with worsening or unchanged symptoms were not. No consistent strategy was identified in the role of lumbar radiographs in the management of low back pain in general practice.

Radiographic examination of the lumbar spine in a community hospital: how many are really necessary?

S. Halpin, L. Yeoman and D. Dundas
Department of Diagnostic Radiology, The Bolingbroke Hospital, London SW11 6HE, UK

The RCR guidelines for the effective use of diagnostic radiation have been introduced into the hospital setting, but are also intended for use by General Practitioners. This study assessed the referral pattern of local GPs for lumbar spine radiography, which represents a substantial radiation dose. One hundred consecutive adult patients completed a questionnaire which evaluated how well their clinical symptoms and signs complied with the guidelines. Their radiographs were assessed for type and severity of abnormality, and this was correlated with symptomatology. Sixty per cent were aged 18–45 years. Thirty per cent had radiologically severe disc or degenerative disease. Four per cent had other diagnoses but there were no cases of malignancy. Five per cent were fully examined by their GP prior to requesting the examination. Nineteen per cent were not examined at all. Only 48% of the examinations complied with the guidelines. Few GPs had heard of the guidelines, but most expressed an interest in them. Many examinations were requested for patient reassurance. The examination result changed the medical management of only a minority of patients. The RCR guidelines need to be more actively promoted within the community, and GPs better informed of the effective use of diagnostic radiation if population dose from this source is to be reduced.

Magnetic resonance imaging myelogram contrast at 0.5 and 1.5 T

T.W. Redpath and S. Wayte
Department of Clinical Physics, Walsgrave Hospital, Coventry CV2 2DX, UK

A magnetic resonance imaging (MRI) myelogram is a T_2-weighted spinal image with TR/TE chosen to give high signal from cerebrospinal fluid with the spinal cord showing grey. Differences in tissue relaxation times between 0.5 T and 1.5 T can cause significant changes in image contrast in conventional spin–echo images, so that TR/TE choices appropriate at one field strength, may not be appropriate at the other. A rampable Picker scanner, capable of operating at 0.5 and 1.5 T, was used to produce multislice T_2-weighted sagittal images of the neck of a normal volunteer, at both field strengths, with TR/TE values of 1600/80, 2000/80, 2000/100 and 2400/100. Results show that shorter TR and shorter TE values can be used at 1.5 T to obtain a given cerebrospinal fluid to spinal cord contrast ratio, than at 0.5 T. This can be partly explained by the increase in T_1 of the cord tissue with field strength, with the T_1 of cerebrospinal fluid remaining constant. Calculations based on the Bloch equations for spin–echo sequences, and changes in tissue T_1 with field strength, predict a smaller effect than that observed.

High dose myelography: the neuroradiological experience

S.F.S. Halpin, P.J. Guest and J.V. Byrne
Department of Radiology, Atkinson Morley's Hospital, Wimbledon, London SW20 0NE, UK

In performing myelography, the radiologist is constrained to inject no more than 3 g of elemental iodine intrathecally by the manufacturers of iohexol and iopamidol. This 3 g maximum intrathecal iodine dose limitation (MIIDL) was arbitrarily carried over from that set for metrizamide, the first non-ionic agent to be used intrathecally, and ignores the superior clinical and toxicological results obtained with the newer agents. In view of the experience at this unit, where up to 6 g have been injected without adverse effects, a questionnaire was sent to 69 members of the British Society of Neuroradiologists to enquire if others shared this experience. Of 46 respondents, 46% always or usually exceed the 3 g MIIDL when performing a myelogram, and a further 39% will do so when they consider a higher dose necessary to produce a diagnostic study; only 15% never inject more than 3 g of iodine. Of the 39 who may exceed the MIIDL, only 10% thought this caused an increase in post-procedure nausea, and 18% thought the high dose may result in excess headache. None believed the high dose to cause an increased incidence of seizures. The 3 g MIIDL is, in practice, clinically irrelevant.

The appearance of posterior osteophytes on high definition computed tomography before and after sound anterior cervical fusions

A.G. Clifton, J.M. Stevens and P. Whitear
Department of Neuroradiology, Maida Vale Hospital, London W9 1TL, UK

Complete removal of posterior osteophytes compressing the spinal cord is not always achieved during Cloward's type procedures on the cervical spine. It has been suggested that this may not be necessary because osteophytes regress after adequate fusion. We have performed high definition computed myelography on 56 patients before and after operations for neurological complications of cervical spondylosis, the second study being performed because the operative outcome was considered unsatisfactory and further surgery was contemplated. In this group were 22 patients in whom sound anterior fusions had been achieved, but residual osteophytes were present. The size and appearance of these osteophytes were carefully compared pre-and post-operatively, the duration between the operation and the second myelogram being 17.4 months mean, range 5 months to 4 years. In 14 patients no differences between the appearances of the osteophytes were shown before and after fusion; in eight cases the change in shape of the osteophytes was best explained by incomplete removal at surgery, not by subsequent remodelling. It was concluded that in this material there was no evidence that posterior osteophytes regress after sound anterior spinal fusion. Every attempt, therefore, must be made to remove all osteophytes at the first operation.

Low back pain in general practice: do lumbar spine radiographs influence patient management?

R. Marsh, J.P. Owen, G. Rutt, M.J. Keir, H. Spencer, D. Richardson, A. Richardson and C. Barclay
Department of Diagnostic Radiology, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne NE1 4LP, UK

One hundred and fifty patients with low back pain were referred by General Practitioners for lumber spine radiographs. Doctors were surveyed immediately before and 6 months after they had received the relevant radiological reports and matched questionnaires were obtained in 65 patients (43%). Symptoms declined with equal frequency in patients both initially receiving and not receiving drug therapy. Fewer patients were on active drug treatment at review. In seven patients initially considered and subsequently sent for second opinions, radiology had no influence on management. In eight patients initially considered but subsequently not sent for second opinions, negative radiology prevented referral of two patients with unchanged symp-

Scientific Programme Abstracts

Monday 29 April

9.00 – 10.15

The Spine

Clarence Room

Intradiscal therapy for the herniated nucleus pulposus in the lumbar spine

I. McCall
Department of Radiology, Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, Shropshire S710 7AG, UK

Intradiscal therapy for herniated nucleus pulposus has been undertaken for many years using Chymopapain. The reports of its efficacy in the literature have shown a degree of variation but more recent studies have indicated that, for the treatment of nerve root compression due to herniation of the nucleus pulposus, following careful clinical and radiological diagnosis can have an expectation of success in 75–80% of cases. Our recent study of 300 cases followed for up to 10 years, had produced similar results. Initial failure is usually due to the presence of a sequestrated fragment of nucleus or to adhesions around the nerve root fixing it to a bulging, partially degenerate, annulus. Longer term problems tend to result from discogenic or facet orientated pain. Recurrent disc herniation is uncommon. The chemonucleolysis denatures the proteoglycans in both the annulus and the nucleus, leading the narrowing of the disc space. At the time of injection it may also produce backache and carries a risk of anaphylaxis. This has stimulated the development of techniques for the percutaneous removal of nuclear material, using small rongeurs or automated suction and cutting devices. The latter have been developed in the USA, where results suggest a similar level of success as for chemonucleolysis. A review of 50 cases undertaken in our institution suggests a slightly lower success rate of 70% and indicates a more restrictive criteria in the selection of patients. Comparative studies of chemonucleolysis and surgery indicate comparable long term results. Similar studies for percutaneous nucleotomy are being undertaken. The use of intradiscal therapy for sciatica due to herniation of the nucleus pulposus offers a real alternative to surgery for those cases where sequestration has not occurred.

The role of magnetic resonance imaging in the assessment of acute and sub-acute cord syndromes

L.A. Mitchell, R.W. Kerslake and B.S.Worthington
Department of Radiology, University of Nottingham, Nottingham NG7 2RD, UK

Eighty-two patients who presented acutely or sub-acutely with focal cord signs have been studied by magnetic resonance imaging (MRI) employing a variety of pulse sequences. Forty-two patients had structural lesions compressing the cord including 27 tumours, eight disc lesions, three cases of atlantoaxial subluxation and an extradural haematoma which were treated by appropriate surgery or radiotherapy. Three extradural abscesses were managed by drainage and antibiotics. In 24 other patients pathology was detected on either the spinal or subsequent brain scan which in the majority allowed a diagnosis to be made (this included multiple sclerosis, cord ischaemia and haematomyelia; in a few, *e.g.* some cases of syrinx, its relationship to the clinical picture was less clear. Sixteen examinations were entirely normal; in several the diagnosis of "myelitis" was clarified by cerebrospinal fluid and serological studies. Surface coil imaging of the spinal column permits high quality thin section studies without planar restriction which gives simultaneous display of soft tissue and bone and avoids patient risk and discomfort. We conclude, therefore, that MRI should replace myelography as the definitive examination in the assessment of acute cord syndromes. It provides the requisite information to direct surgery and radiotherapy planning; more significantly, it allows recognition of pathological changes within the cord substance.

NORFOLK ROOM

RADIATION PROTECTION

Chairman: Mr D Gifford, Bristol

2.30-2.50 *Invited Review*	**Implications of the new ICRP recommendations for medical radiology** Dr R H Clarke, NRPB, Chilton *(p.107)*
2.50-2.58	**Normalised scattered radiation data for diagnostic radiology equipment** N W Marshall, Newcastle-upon-Tyne *(p.107)*
2.58-3.06	**Is some of our dosimetry wrong?** P Dawson, London *(p.107)*
3.06-3.14	**Coronary angiography: An analysis of UK patients** L P Readman, Manchester *(p.107)*
3.14-3.18	**I-131 labelled mIBG therapy for neuroblastoma in young children - radiation doses received by parents and other relatives** S Packer, Leeds *(p.108)*
3.18-3.22	**Doses to radiologists doing cardiac catheterisation procedures** C Taylor, Leeds *(p.108)*
3.22-3.26	**Radiation doses to paediatric patients undergoing special radiographic procedures** C L Chapple, Newcastle-upon-Tyne *(p.108)*
3.26-3.30	**Radiation dose to patient and personnel in extracorporeal shock wave lithotripsy** C Baldock, London *(p.108)*
3.30-3.34	**Radiation dose to the eye and thyroid gland in high resolution computed tomography of the pituitary gland** L P Readman, Manchester *(p.109)*
3.34-3.38	**Use of a database to analyse patient doses from radiographic examinations and assist in their reduction** C J Martin, Aberdeen *(p.109)*
3.38.3.42	**Evaluation of a diamentor** G D Morrison, London *(p.109)*

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Ultrasound in the diagnosis of the juxta-pleural lesion

By M. J. Bradley, MB ChB, FRCR and C. Metreweli, FRCP, FRCR

Department of Diagnostic Radiology and Organ Imaging, Prince of Wales Hospital, Hong Kong

(*Received May 1990 and in revised form August 1990*)

Keywords: Ultrasound, Juxta-pleural lesions

Abstract. Any opacity on a chest radiograph has a wide differential diagnosis. Plain radiography and computed tomography may help to differentiate whether bone, intercostal soft tissue or mediastinum are involved. Bronchoscopy is often negative with peripheral lesions. This leaves the physician with a diagnostic problem. We examined ultrasonically 30 patients with juxta-pleural lesions and performed cutting biopsy in 27. Twenty-four of these produced positive histology (90%). The three that were not biopsied were anechoic and had pulsatile lesions due to vascular abnormalities. There were four benign lesions all with hypo-echoic appearances and the 20 malignant cases showed a wide spectrum of echogenicity. Of the malignant lesions, 90% showed pleural line disruption with reduced respiratory movement suggesting chest wall invasion. There were no complications, despite using cutting biopsy.

We were stimulated to conduct this study because of our high local incidence of tuberculosis and primary lung tumours. Clinicians need to know whether the patient has dual pathology, or whether the disease is benign or malignant so that he can initiate appropriate treatment.

In order for ultrasound to be of help in this assessment, the lesion must be juxta-pleural. Yang et al (1985) have described different echogenicities in the lesions but we wanted to compare this with the histology in order to establish a pattern. The visceral and parietal pleurae can be seen ultrasonically (Saito et al, 1988) and we have used this sign, together with reduced movement, as an indicator of chest wall invasion. This can be compared with loss of the fat plane which can be clearly seen on computed tomography (CT).

Patients and methods

Thirty consecutive patients who had a juxta-pleural lesion on postero-anterior (PA) and lateral chest radiographs with negative bronchoscopy underwent sonography.

The study was carried out on an Aloka 650 using 3.5 and 5 mHz convex linear probes with occasional use of a 5 mHz sector probe to look at smaller lesions between the ribs. Most examinations were performed with the patient lying down, but use of the erect position occasionally enabled the use of improved intercostal windows. The echotexture, size and shape of the lesion, together with its movement and disruption of the pleural line, were assessed.

Using Trucut needles and an aseptic technique, 27 lesions were biopsied; three biopsies were contraindicated on the ultrasound appearances. Ultrasound resulted in an accurate needle placement in each case.

All patients had a post-procedure erect expiratory chest radiograph to exclude a pneumothorax.

Results

Thirty patients were examined sonographically. The male to female ratio was 2:1 with a mean age of 59 years (range 3–83 years).

With only one exception, the chest radiographs showed solitary lesions, twice as many occurring on the right as the left. The patient with multiple lesions was thought to have pleurally based metastases on the chest radiograph, which proved to be due to thymic carcinoma on biopsy. Only five patients had concurrent pleural effusions. The PA chest radiograph showed the majority of the lesions lay peripherally in the mid-axillary line (14) with a further six in the apices, three basal and six central. The lateral film showed four central lesions to be adjacent to the posterior chest wall and two anteriorly. The remaining patient with thymic carcinoma had pleurally based lesions scattered through the left hemithorax.

The lesions were identified sonographically and they varied from 1 cm to 10 cm in size. We could see several lesions in the patient with the thymic carcinoma and the largest and most accessible was biopsied.

Three lesions were anechoic and pulsatile and so were considered to be vascular abnormalities and therefore did not undergo biopsy (Fig. 1). Contrast-enhanced CT confirmed aneurysms of the brachiocephalic artery, arch of aorta and an arteriovenous malformation of the pulmonary vein. At surgery, the last lesion was due to a tumour thrombus dilating the pulmonary vein.

The remaining lesions had varying echogenicity compared with the intercostal muscles and this is summarized in Table I. All the benign lesions were hypo-echoic while malignancy demonstrated any pattern (Fig. 2).

Address for correspondence: Dr M. J. Bradley, c/o Department of Radiodiagnosis, Royal Liverpool Hospital, P.O. Box 147, Liverpool L69 3BX.

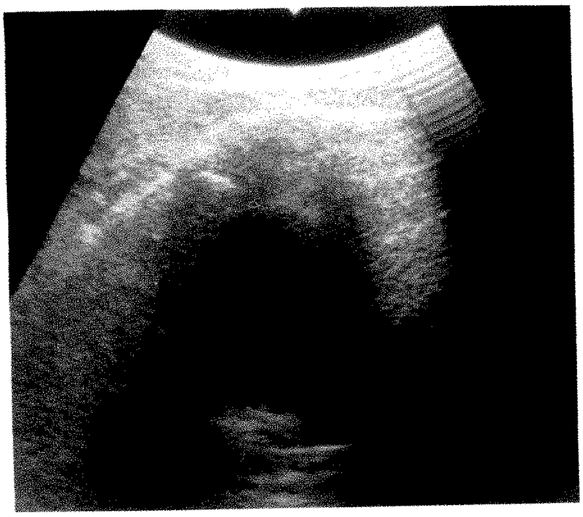


Figure 1. Ultrasound of this central mass shows it to anechoic and pulsatile, typical of a vascular structure. Surgery proved this to be a pulmonary vein dilated by tumour thrombus.

Table I. Spectrum of echogenicities of the 27 biopsied lesions

	Malignant ($n = 20$)	Benign ($n = 4$)	Non-specific ($n = 3$)
Hypoechoic	5	4	2
Isoechoic	4	—	1
Hyperechoic	7	—	—
Complex	4	—	—

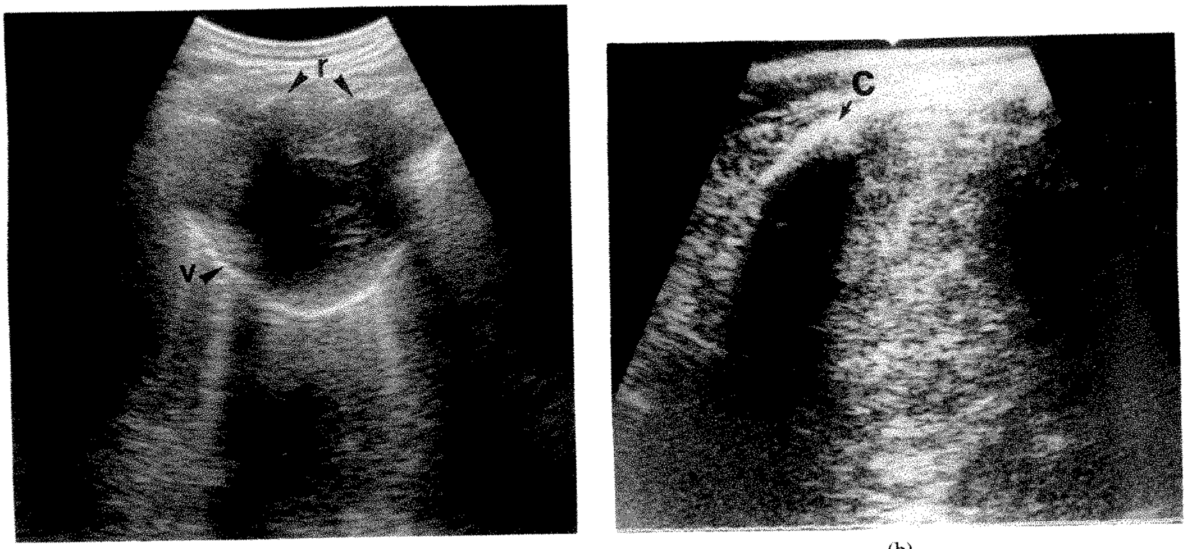
Three biopsies revealed non-contributory tissue on each of two occasions. These patients were followed up and showed no change in their condition or chest radiograph features at 6 months. We therefore presume these lesions to be of little clinical significance.

Our biopsy technique yielded positive histology in 24 patients (90%). The range of malignant histology is summarized in Table II.

Three of the four benign lesions were due to tuberculosis (TB) and the fourth was a plasma cell granuloma (inflammatory pseudotumour). Only one patient had dual pathology: one man with acid fast bacilli in his sputum and an apical mass which proved to be a squamous cell carcinoma on biopsy.

The radiographic shape may lead the radiologist to infer that the lesion is pulmonary or pleurally based. Similarly, ultrasound of intra-pulmonary lesions usually shows a round lesion with acute angles formed at its wall and pleural lines (Fig. 3). Tapered lesions with obtuse pleural/lesion angles are usually pleurally based (Fig. 4). This correlated well with the tissue type as all the round lesions comprised primary lung tissue tumours and only one of the tapered lesions contained lung tissue.

The pleural lines were identified in each case and were either intact or disrupted by the mass. Of the 20 malignant cases, 18 had pleural disruption ultrasonographically (90%) whilst only one benign lesion, due to TB showed the same sign. Suspended respiration aids detail of the pleural line disruption, but it is important to assess the movement of the lesion in relation to the chest wall. Round, mobile lesions are intrapulmonary, whilst if tapered and fixed, these are pleurally based.



(a)

(b)

Figure 2. (a) Complex mass proven to be a squamous cell carcinoma. Parietal pleura disrupted with intact visceral pleura (r = rib, v = visceral pleura). (b) Hyperechoic mass seen between the ribs due to an adenocarcinoma (c = clavicle).

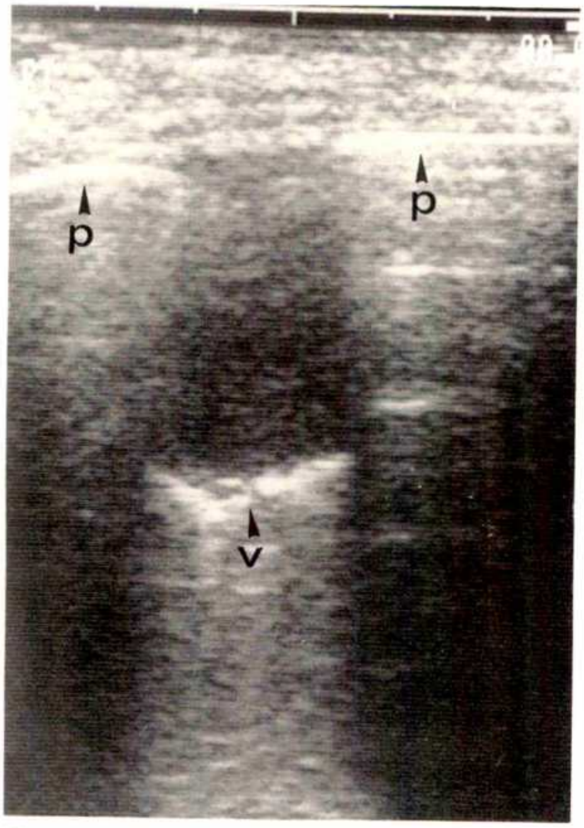


Figure 3. The ultrasound demonstrates a round hypo-echoic lesion with disrupted parietal pleural line indicating chest wall invasion confirmed at surgery (p = parietal pleura, v = visceral pleura).

Round, fixed lesions with pleural line disruption indicates chest wall invasion. We observed reduced movement in each of our 18 malignant cases with pleural line disruption.

We observed no immediate or delayed complications and we attributed this to the lesions being peripheral and to the high degree of confidence that the needle was solely within the lesion as a result of ultrasound guidance.

Table II. Histology range in 23 malignant biopsies out of a total 27 biopsies

Adenocarcinoma	6
Adenosquamous	1
Squamous	7
Small cell	1
Spindle cell	1
Large cell	1
Pleural secondary deposit from malignant thymoma	1
B-cell non-Hodgkin's lymphoma	1
Infantile fibrosarcoma	1
Total	20

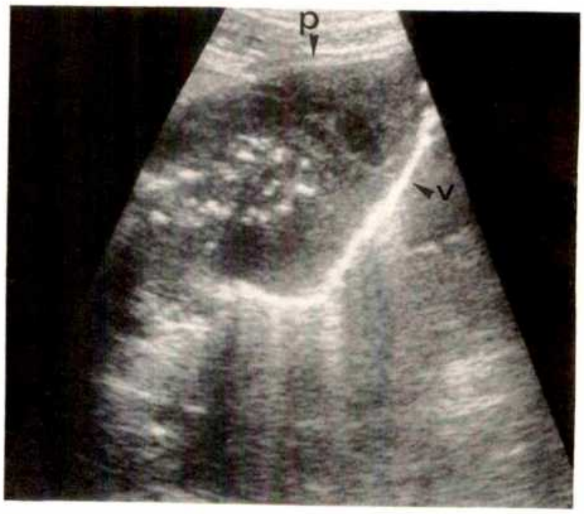


Figure 4. Pleurally based tapered complex mass due to B cell non-Hodgkin's lymphoma (p = parietal pleura, v = visceral pleura).

Discussion

The clinical question as to whether the lung lesions in our cases were benign or malignant tumours or tuberculosis was answered in 90% of cases by ultrasound imaging and guided biopsy. Singh et al (1987) also described similar positive histology results with juxta-pleural lesions.

The echotexture of juxta-pleural lesions showed a wide range of echopatterns. Twenty malignant tumours demonstrated all types of echogenicity as compared to that of the intercostal muscle. Whereas all seven benign lesions were echopoor including, not surprisingly, the vascular abnormalities which were anechoic and pulsatile.

Seventy-five per cent of the malignant lesions were isoechoic, hyperechoic or complex. Thus, from our results, it would appear that, if the lesion is echopoor, it is difficult to predict benignity or malignancy. However, other echogenicities are seen then 94% of these can be expected to be malignant.

Saito et al (1988) described the visceral and parietal pleural lines sonographically as thin echogenic lines. If the parietal pleura is disrupted around the lesion and there is reduced movement of the lesion in relation to the chest wall, then we may conclude that there is chest wall involvement. However, only six patients with malignancy were felt to have surgically resectable lesions. We accurately predicted chest wall involvement in these cases but are unable to correlate the remainder. Our one case of TB demonstrating pleural line disruption leading to a false positive impression of malignancy may be explained by the inflammatory nature of the lesion.

Our results suggest that when there is pleural line disruption with reduced respiratory movement of the lesion then 90% will be malignant.

The lesion in the child with infantile fibrosarcoma was so large that we felt that it was not possible to assess pleural disruption completely and we assume that this is the reason why we failed to show pleural involvement in this case.

We conclude, therefore, that appraisal of the echogenicity of the lesion and pleural line disruption is an accurate indicator of malignancy.

Saito et al (1988) and Hirsch et al (1987) have described the shapes of the lesions. Sonography reflects that shape seen on the chest radiograph and may help to determine whether the lesion is that of pulmonary, chest wall or pleural in origin. Seventeen of 20 malignant lesions appeared round and histology showed primary intrapulmonary tumours. Tapered lesions suggest a chest wall or pleural lesion, and does not necessarily equate with chest wall malignant invasion as most of our benign lesions had this shape. It is more important to identify the intact visceral and parietal pleural lines.

Haller et al (1980) have previously reported "through transmission" with various lesions. We have found this an impossible sign to identify as the ribs cast an acoustic shadow around the lesion and even in the plane between the ribs it was difficult to visualize transmission due to the high lung reflectivity.

Negative tissue biopsies always raise the possibility of a geographical miss in the sampling or an inappropriate part of the lesion having been sampled. With direct visualization during ultrasound guided biopsy, the needle is demonstrably within the lesion. Heterogeneous lesions can be sampled from the most solid area or different areas of echogenicity. This was certainly the case in our tumour with a necrotic fluid centre in which we were able to sample the solid wall, which might have been missed using other imaging modalities.

Several authors including Cheng et al (1986), Yang et al (1985) and Pederson (1986) have used fine needle aspiration techniques with ultrasound or fluoroscopy imaging. This is considered to be less hazardous but is dependent on a good cytological service, which is not available in all hospitals. Also, fine needles are more difficult to follow with ultrasound than the thicker cutting needles. This is because the thin needles do not generate as large a signal and are more likely to be deflected from the target path. Being able to make a "direct hit" makes the use of thick needles for juxta-pleural lesions as safe as the use of fine needles, as our complication rate suggests. Also, FNA may not be able to describe histology of the tumour which is available on a tissue core (Pang et al, 1987).

Conclusion

Sonographic evaluation of the juxta-pleural mass has proved extremely useful in the diagnosis of such a lesion. Its shape and movement help to determine pulmonary from pleurally based lesions and the echogenicity may aid benign malignant differentiation. We believe that pleural line disruption with poor respiratory movement is a sign of chest wall invasion.

Ultrasound is a safe and accurate imaging medium for biopsy guidance.

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Evaluation of the use of a niobium filter for patient dose reduction in chest radiography

By H. Thierens, PhD, *M. Kunnen, MD, PhD, A. Van der Plaetsen, MS and O. Segaert, PhD

Department of Medical Physics, University of Ghent, Proeftuinstraat 86, and *Department of Radiology, University Hospital Ghent, De Pintelaan 185, B-9000 Ghent, Belgium

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Abstract. The performance characteristics of a 50 μm niobium filter and a copper filter of equivalent thickness (0.15 mm) were compared for postero-anterior chest X-ray examination. Radiographs of 20 patients obtained using an automatic exposure control device showed no significant differences in image quality and exposure setting between the filters. Radiation dose distributions measured in a Rando phantom revealed a higher reduction in the patient dose with the niobium filter. The reduction in the effective dose equivalent, produced by the addition of the niobium and copper filters to the standard filter of 2.5 mm aluminium, of 17% and 10%, was relatively small compared with the reductions in the entrance surface dose of 31% and 26%. Our study confirms that drastic alterations in the patient dose by the addition of a dose reduction filter to the usual filtration cannot be expected.

The radiation quality of an X-ray beam emerging from a particular X-ray tube with given anode material is determined by the potential applied to the tube and the total filtration. The choice of these parameters for a specific radiographic projection is based not only on the image quality, providing the necessary diagnostic information, but also on the absorbed dose delivered to the patient. Owing to the somatic and genetic risks associated with exposure to ionizing radiation, the patient dose has to be kept as low as is reasonably achievable (ALARA principle).

For a specific radiographic projection with appropriate tube potential, the radiation dose to the patient is reduced by an increase in the filtration of the beam. In the ideal situation, the strongest filtration without loss of image quality is the optimal choice. However, an increase in filtration reduces the useful output and necessitates an increase in the tube current–exposure–time product (mA's value) to obtain the same optical density in the radiograph. Consequently, a reduction in the patient dose is inevitably associated with an increase in the tube load.

As a compromise, taking into account both the dose reduction to the patient and additional costs inherent in the higher tube load, combinations of fixed tube potential and aluminium filtration are used in practice in radiological departments. Minimum values for the total filtration are recommended in the ICRP publication 34 (1982).

According to different authors (Villagran et al, 1978; Burgess, 1981; Chakera et al, 1982; Wesenberg et al, 1983; Wang et al, 1984; Burgess, 1985; Tyndall & Washburn, 1987), the addition of a thin metal foil of a rare earth material, a so-called dose reduction filter, to the existing aluminium filtration can substantially reduce the dose to the patient without having any noticeable detrimental effect on the image contrast. These filters are also called K-edge filters. However, only the heavy rare earth metals such as erbium and gadolinium have their K absorption edge around 50 keV, the central part of the X-ray spectrum, and can act as bandpass filters in general diagnostic radiology. Light earth metals such as yttrium, niobium and molybdenum have their K absorption edge around 20 keV, which is too low, and can only be considered as conventional filter materials.

The conclusions on patient dose reduction are partly based on measurements of the entrance surface dose, without taking into account the reduction in the air-kerma at the image receptor, requiring a significant increase in exposure setting to obtain the same optical density on the film.

Calculations of the integral absorbed dose and the effective dose equivalent performed by Koedooder and Venema (1986), Shrimpton et al (1988) and Nagel (1989) showed only small reductions in the patient dose. Furthermore, Nagel (1989) claimed that rare earth filters offer no significant advantages over ordinary iron and copper filters. The conclusions of these authors leave the merits of the so-called dose reduction filters very controversial.

We evaluated the performance characteristics of the commercially available NIOBI-X filter from RadRed Laboratories for postero-anterior (PA) projection of the chest, the most common X-ray projection. This dose reduction filter consists of a 50 μm thick layer of niobium ($Z = 41$) encased in plastic to prevent oxidation. Changes in image quality, effective dose equivalent delivered to the patient and exposure setting caused by the addition of the filter were studied experimentally. According to the information material supplied by the manufacturer (RadRed Laboratories, 1988), an entrance dose reduction of between 35% and 45%, depending on the existing aluminium filtration, can be expected with the addition of the 50 μm NIOBI-X filter to the filter assembly for high voltage radiography without affecting the image contrast.

In view of the conclusions of Nagel (1989), the characteristics of the niobium filter were also compared with those of a copper filter with an equivalent thickness (with reference to the radiation quality specified by the half-value layer (HVL), measured in millimetres of aluminium).

X-ray source and radiation qualities used

The X-ray unit used for the evaluation of the niobium filter was a Thoramat (Siemens) of the Radiology Department of the University Hospital Ghent. This unit consists of a Tridoros 172 MP generator coupled to an Optilix rotating anode tube. The Thoramat, designed for chest examinations, allows automatic development of the films. The exposure time is determined by an automatic exposure control device with three ionization chambers. In the experiments, the mA's value was measured with a Fluke 8000A digital multimeter inserted in the anode circuit. A Titan 2U(Siemens)–XLA(3M) film–screen combination was used. The field size at the image receptor was 40 cm × 40 cm. The potential applied to the tube was 141 kV, the value used in the hospital for chest examinations with the high voltage technique. The effect of the addition of the 50 μm thick niobium filter to the total filtration of 2.5 mm aluminium in daily routine was studied for this value of potential. To compare the performance characteristics of this dose-reducing filter with an ordinary copper filter, the niobium filter was replaced by a copper filter with equivalent thickness, *i.e.* 0.15 mm.

The HVL values of the radiation qualities used are summarized in Table I. They were determined experimentally using an NE2571 thimble ionization chamber coupled to a 2570 Farmer dosemeter (NE-Technology). The distance from the source to the image receptor was 2 m.

Table I. Effect of dose reduction niobium and equivalent copper filters on HVL and mA's values for a single PA chest exposure; the density values at the four points indicated in Fig. 1, average over all patients, are also included

	Filtration		
	2.5 mm Al	+50 μm Nb	+0.15 mm Cu
HVL (mm Al)	4.5	7.4	7.3
mA's value	10.4	12.7	12.6
Density A	0.77	0.75	0.75
B	1.35	1.36	1.38
C	1.10	1.06	1.04
D	0.33	0.31	0.31

Image quality and tube load

To evaluate possible detrimental effects on the image quality and the increase in tube load caused by the introduction of the niobium filter and the copper filter with equivalent thickness, three consecutive chest radiographs were taken of 10 male and 10 female patients: one with the usual 2.5 mm aluminium filter, one with a 50 μm niobium dose reduction filter added to the 2.5 mm aluminium filter, and one with the niobium filter replaced by a 0.15 mm copper filter. Patients were selected so that a population covering all patient sizes and age groups was obtained for the study. Informed consent was obtained from each patient. The patient was told to remain in the same position and to try to take the same deep breath during the three exposures.

The average mA's values of the resulting radiographs, obtained using an automatic exposure control device, are also summarized in Table I. The addition of the niobium filter necessitated an increase in the exposure setting of 22(4)%, and the addition of the equivalent copper filter necessitated an increase of 21(4)%. The uncertainties are given in brackets and represent the standard deviations for the considered heterogeneous population. The small value of standard deviation, 4%, shows the reproducibility of the difference in exposure setting between the different filtration conditions.

To highlight the effect of the dose reduction niobium and equivalent copper filters on the image quality, the radiographs were analysed separately by five experienced practising clinical radiologists. After encoding, each triplet of radiographs (2.5 mm aluminium filtration, niobium filter added and copper filter added) was scored for overall image contrast and detailed diagnostic information. The results of this evaluation for the 20 patients considered in the study are summarized in Table II.

In all patients the radiograph without additional filtration was claimed by all five observers to present the highest overall contrast; the differences, however, were described as very small. Furthermore, the scoring system revealed no observable difference in contrast between the radiographs obtained with the additional niobium and copper filters: in 55% of assessments the radiograph obtained with the niobium filter was thought to present the lowest contrast, and in 45%, the copper filter was thought to yield the lowest contrast. There was high interobserver variability. Further details can be found in Table II.

In addition to evaluation of the overall contrast by the viewing panel, an objective comparison was performed by densitometry of the chest radiographs in confined regions of low and high optical density. The regions selected for this comparison are indicated in the radiograph shown in Fig. 1: the aortic knob (A), the lung parenchyma in the opposed costal interspace (B), the right supradiaphragmatic lung parenchyma (C) and the shadow of the left ventricle (D). Attention was paid to ensure that the densities were not measured at the levels of superposing ribs, small pulmonary vessels or bronchi. As parameters representative of the objec-

Table II. Effect of dose reduction niobium and equivalent copper filters on the image quality

Patient	Sex	Lowest contrast					Diagnostic value									
							First choice					Second choice				
		Observer					Observer					Observer				
		1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
1	M	Cu	Cu	Cu	Nb	Cu	Cu	no	Nb	no	Cu	Nb	Nb	Cu	Cu	Nb
2	M	Nb	Nb	Cu	Nb	Cu	Cu	no	Nb	no	no	Nb	Cu	Cu	Cu	Cu
3	M	Nb	Cu	Cu	Nb	Cu	Nb	no	Cu	no	Cu	Cu	Nb	Nb	Cu	Nb
4	F	Nb	Nb	Nb	Nb	Nb	Cu	no	no	Cu	Cu	Nb	Nb	Cu	Nb	Nb
5	F	Nb	Nb	Cu	Nb	Nb	Cu	no	Cu	no	Nb	Nb	Cu	Nb	Cu	Cu
6	F	Cu	Cu	Nb	Nb	Nb	Nb	Cu	no	Cu	no	Cu	Nb	Cu	Nb	Cu
7	M	Cu	Nb	Cu	Cu	Nb	Nb	Nb	Nb	Nb	Nb	Cu	Cu	Cu	Cu	Cu
8	F	Nb	Nb	Cu	Cu	Nb	no	no	Nb	no	Nb	Nb	Nb	Cu	Nb	Cu
9	F	Nb	Cu	Cu	Cu	Cu	no	Nb	no	Nb	no	Nb	no	Nb	Cu	Cu
10	F	Cu	Nb	Nb	Nb	Cu	Cu	Nb	no	Cu	Nb	Nb	Cu	Cu	Nb	Cu
11	M	Nb	Nb	Nb	Nb	Cu	Nb	Cu	no	Cu	Nb	Cu	no	Nb	Nb	Cu
12	F	Cu	Nb	Nb	Cu	Cu	no	Cu	Nb	Nb	Nb	Nb	no	Cu	Cu	Cu
13	M	Cu	Cu	Nb	Cu	Cu	no	Nb	Nb	Nb	Nb	Nb	no	Cu	Cu	Cu
14	M	Nb	Nb	Nb	Nb	Nb	no	no	Cu	no	no	Nb	Nb	Nb	Nb	Nb
15	M	Nb	Nb	Cu	Nb	Nb	Nb	Cu	Nb	no	Nb	Cu	Nb	Cu	Cu	Cu
16	F	Nb	Cu	Cu	Cu	Nb	no	Nb	Nb	Cu	no	Nb	Cu	Cu	Nb	Nb
17	F	Cu	Cu	Cu	Cu	Nb	Cu	Nb	Cu	Nb	no	Nb	Cu	Nb	Cu	Nb
18	M	Nb	Cu	Nb	Cu	Nb	Nb	Cu	Cu	no	Cu	Cu	Nb	Nb	Nb	Nb
19	F	Nb	Nb	Nb	Nb	Cu	Cu	Cu	Cu	Cu	Nb	Nb	Nb	Nb	Nb	Cu
20	M	Nb	Cu	Cu	Cu	Nb	Cu	Nb	no	no	Nb	Nb	Cu	Nb	Nb	Cu
Summary				Nb 55/100 Cu 45/100					Nb 36/100 Cu 30/100 no 34/100					Nb 49/100 Cu 47/100 no 4/100		

Key: no, 2.5 mm Al filtration; Nb, 2.5 mm Al + 50 μm Nb filtration; Cu, 2.5 mm Al + 0.15 mm Cu filtration.

tive contrast, the differences in optical density between regions A and B and regions C and D for the three filtrations are plotted against patient number in Fig. 2. The full, dashed and dotted lines represent the values obtained by averaging over all the patients for 2.5 mm aluminium filtration, and additional niobium and copper filters respectively. Taking into account all the data presented in Fig. 2, we can conclude that, based on densitometry of discrete confined regions, systematic differences in contrast between the three filtration conditions cannot be observed.

The densitometry also showed that the radiographs produced by the different filtrations with the mA's values given in Table I were of comparable overall density. The density values at the four points indicated in Fig. 1, obtained by averaging over the 20 patients, are listed in Table I. In view of these results, the dose reductions produced by the additional niobium and copper filters, as reported in this paper, cannot be attributed to differences in overall density of the radiographs owing to the X-ray energy dependence of the automatic exposure control.

Concerning detailed diagnostic information, the evaluation by the radiologists showed the equivalence of the different filtrations: the niobium filter was selected 36 times as first choice, the copper filter 30 times and the usual 2.5 mm aluminium without additional filtration 34 times. More details can be found in Table II. For this evaluation, special attention was first focused on the delineation of the smaller structures such as the segmental bronchi and the pulmonary blood vessels. As a second step, the less clear or more clear delineation of structures such as the trachea, the carina, the left main bronchus and the descending aorta was assessed.

In conclusion, except for a possible small reduction in overall contrast, the use of a dose reduction niobium filter or equivalent copper filter does not degrade the image quality.

Radiation dosimetry

Radiation dose distribution measurements were made using thermoluminescent dosemeters (TLDs) placed in an anthropomorphic (average man) Rando phantom marketed by Alderson Research Laboratories (USA). We used lithium fluoride (TLD-700 Harshaw) extruded chips (0.10 cm^2 in area, 0.09 cm thick) as TLDs. They were preselected to have a sensitivity within 3% of the mean value. The selected TLDs were calibrated free in air against the NE2571 thimble ionization chamber. The calibration was performed at the same radiation quality

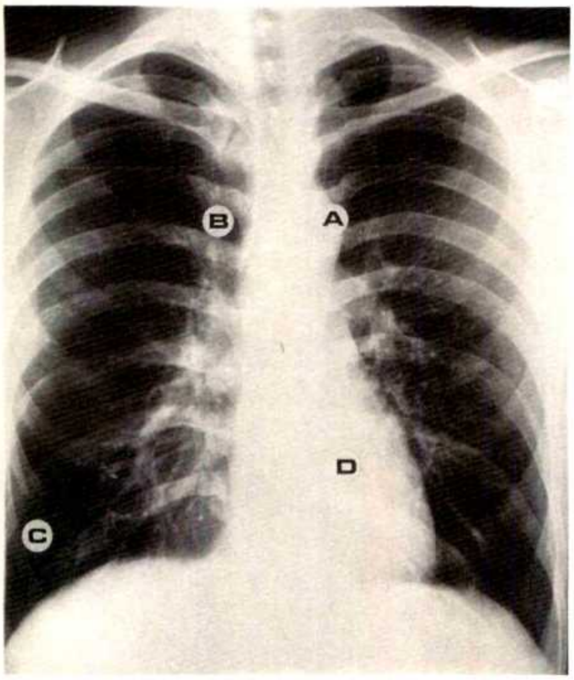

Figure 1. Chest radiograph of Patient 2 with 2.5 mm aluminium plus 0.15 mm copper filtration. The regions used for a comparison of the contrast between the different filtration conditions by film densitometry are indicated.

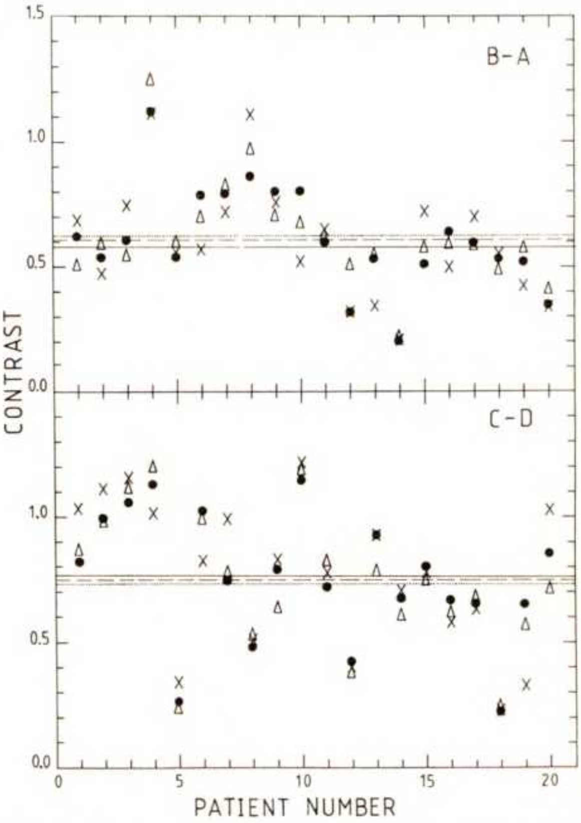

Figure 2. Contrast values between regions A and B (upper part) and regions C and D (lower part) shown in Fig. 1, plotted against patient number for the usual 2.5 mm aluminium filtration (X), plus a 50 μm niobium filter (●) and plus an 0.15 mm copper filter (△). The mean values, obtained by averaging over all patients, are indicated by the full line (2.5 mm aluminium), the dashed line (+ 50 μm niobium) and the dotted line (+ 0.15 mm copper).

used for the *in situ* dosimetry. The NE2571 ionization chamber was calibrated against a standard free-air ionization chamber in the Medical Physics Laboratory for a radiation quality generated by a peak tube potential of 120 kV and a total filtration of 4 mm aluminium, corresponding to an HVL of 5.0 mm aluminium. The reproducibility of the TLDs was investigated in a separate experiment.

An average value of 1.2% was obtained for the standard deviation of replicate readings of the same chip.

For evaluation of the patient dose, the calibrated TLDs were located in the Rando reference phantom at representative sites corresponding to radiosensitive organs and tissues. The same TLD–phantom location combinations were used for the comparative niobium and copper studies.

The choice of the sites was based on a complete computed tomography scan series of the phantom. A total of 10 dosemeters were distributed over both lungs. For the determination of the dose to the total active bone marrow, the distribution of the active bone marrow over the skeleton was taken into consideration (Ellis, 1961). The contribution of the different skeletal regions in the direct beam to the marrow dose was measured by locating TLD chips in the ribs (10), in the sternum (four) and in the cervical and thoracic spine (six). Adopting the data of Ellis, 25.8% of the total active bone marrow (7.9% in the ribs, 2.2% in the sternum, 1.6% in the clavicles, 17.5% in cervical and thoracic vertebrae) was assumed to be in the primary beam. The average skin dose was derived from the readings of 12 dosemeters located at the anterior, posterior and lateral phantom skin. Finally, two dosemeters were used for an estimation of the dose to the testes from scattered radiation.

A cross-section of the phantom indicating the positions of the dosemeters in the horizontal plane located at Rando slice 16 and the sixth thoracic vertebra is shown in Fig. 3.

Thermoluminescent dosemeter exposure readings for the internal organ sites were converted to the dose absorbed in tissue using the *f*-factor for striated muscle, given as a function of HVL value and peak tube potential in a previous paper (Seuntjens et al, 1987).

To obtain dose measurements with a sufficient accuracy well above the detection limit of LiF TLDs

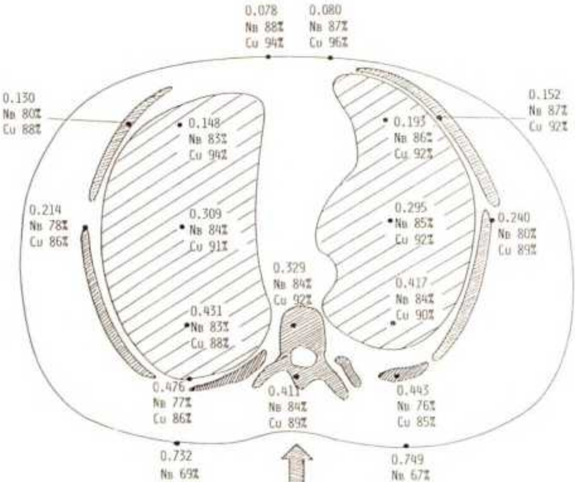

Figure 3. Dose values (in mGy) at representative sites in the phantom cross-section at Rando slice 16 for a single PA chest radiograph with the usual filtration of 2.5 mm Al. To highlight the dose reduction, absorbed dose values obtained by the introduction of 50 μm niobium and 0.15 mm copper filters are expressed as a percentage of the 2.5 mm aluminium filtration doses.

(50 μSv), the dose distributions were obtained with an exposure setting corresponding to 100 times the mA's value given in Table I.

The dose values for the usual filtration of 2.5 mm aluminium are indicated in Fig. 3. In addition, doses absorbed with the introduction of the niobium and copper filters are given. These values are expressed as a percentage of the 2.5 mm aluminium filtration dose.

Average absorbed doses to the organs and parts of the skeletal structure for the different filtrations considered in the study are compared in Table III. The values in Fig. 3 and Table III refer to a single PA chest X-ray examination with the mA's values given in Table I. The errors indicated in brackets are derived from standard deviations of the TLD readings.

Introduction of the 50 μm niobium filter results in a reduction in the patient dose by 31% at the entrance skin, decreasing in the body to 12% and 9% at the exit skin and sternum respectively. The same pattern is found for the copper filter of equivalent thickness (0.15 mm) but the dose reducing effect is about 6% less for all dosemeter sites.

Discusssion

According to the information supplied by the manufacturer (RadRed Laboratories, 1988) a reduction in the patient exposure of between 35% and 45% can be expected for high voltage radiography when using an additional NIOBI-X filter. These values are derived from entrance surface dose measurements. In our study, a skin sparing effect of 31% was also observed. However, owing to the strong attenuation of the X-ray beam in the patient, a reliable assessment of the radiological risk for the patient cannot be deduced from the entrance surface dose. Instead of this parameter, the effective dose equivalent H_E is currently considered as being the most appropriate indicator of the patient risk in medical radiation dosimetry (UNSCEAR, 1982).

The concept of the effective dose equivalent was introduced by the ICRP to deal with non-uniform radiation exposure in radiation protection practice. In ICRP publication 26 (1977), the effective dose equivalent H_E, defined by the expression

$$H_E = \sum_T W_T H_T$$

is the dose equivalent resulting from uniform irradiation of the whole body giving the same stochastic risk as the considered non-uniform exposure. In this expression, H_T is the dose equivalent delivered to tissue T and W_T is the weighting factor representing the proportion of the stochastic risk resulting from tissue T to the total risk for uniform whole body irradiation. The stochastic risks considered in the concept of H_E are the risk of fatal cancer and the risk of serious genetic disorders in the first two generations. It is evident that an evaluation of the dose reduction properties of different filters has to be based on the values of the effective dose equivalent and not on the entrance surface dose values.

Dose equivalent values to the radiosensitive tissues and organs considered in ICRP publication 26 (1977), together with the resulting effective dose equivalent due

Table III. Doses to organs and tissues (mGy) for a single PA chest radiograph

Tissue	Filtration		
	2.5 mm A1	+50 μm Nb	+0.15 mm Cu
Ribs	0.276 (0.006)	0.218 (0.005)	0.241 (0.005)
Sternum	0.100 (0.005)	0.091 (0.005)	0.097 (0.005)
Spine	0.389 (0.013)	0.329 (0.011)	0.349 (0.012)
Lung	0.282 (0.005)	0.239 (0.004)	0.257 (0.004)
Thyroid	0.145 (0.006)	0.120 (0.005)	0.133 (0.005)
Skin entry	0.740 (0.026)	0.507 (0.018)	0.546 (0.020)
Skin exit	0.078 (0.003)	0.069 (0.003)	0.074 (0.003)
Testes	< 0.001	< 0.001	< 0.001

Table IV. Effective dose equivalent (mSv) for a single PA chest radiograph

Tissue	Filtration			W_T
	2.5 mm Al	+50 μm Nb	+0.15 mm Cu	
Gonads	0.0	0.0	0.0	0.25
Breasts	0.078 (0.003)	0.069 (0.003)	0.074 (0.003)	0.15
Active bone marrow	0.081 (0.004)	0.067 (0.003)	0.073 (0.003)	0.12
Lung	0.282 (0.005)	0.239 (0.004)	0.257 (0.004)	0.12
Thyroid	0.145 (0.006)	0.120 (0.005)	0.133 (0.005)	0.03
Bone surface	0.044 (0.003)	0.036 (0.002)	0.038 (0.002)	0.03
Remainder	0.083 (0.005)	0.065 (0.004)	0.070 (0.040)	0.30
H_E	0.086 (0.004)	0.071 (0.003)	0.077 (0.003)	

to a PA chest X-ray examination with and without niobium and copper filters are compared in Table IV. The uncertainties of the dose equivalent values are given in brackets.

As pointed out by Huda and Sandison (1988) the procedure proposed by the ICRP for the determination of the "remainder" component of H_E, representing the radiological risk associated with doses to organs not explicitly listed as radiosensitive organs, poses a number of practical difficulties in diagnostic radiology. For the assessment of this component we adopted the alternative approach proposed by Huda and Sandison (1988) based on the assumption that the risk for the "remainder" is simply proportional to the irradiated mass. The tissue distribution data of the Rando phantom reported by Huda and Sandison (1984) were used in the calculation of the irradiated mass. The same procedure was followed for the assessment of the dose equivalent to the bone surface. For the breast dose, the anterior skin dose was adopted.

Table IV shows that a dose reduction effect of 17% is obtained by introduction of the 50 μm niobium filter, significantly less than the 31% derived from entrance surface dose measurements and the 35–45% given in the information material (RadRed, 1988). The observed effect is of the same magnitude as the numbers quoted by Nagel (1989) as the maximum dose reduction which can be expected by optimizing the filtration of the X-ray beam (20–30%). The benefit of a reduction of the patient dose by 17% has to be paid for by an increase in tube load by 22% to obtain the same density. This increase in tube load is small compared with the increase in exposure setting required by the introduction of rare earth erbium and ythrium filters, calculated by Shrimpton et al (1988) for PA projection of the chest, which is typically 200%. Following the Monte Carlo calculations performed by these authors, the reduction in the effective dose equivalent by these filters is only 10%. The performance characteristics of a 50 μm niobium filter are clearly better than would be expected from the results of Shrimpton et al (1988).

A copper filter with equivalent thickness according to the equal HVL aluminium criterion reduces the patient dose by 10% and requires an increase in tube load of 21%, very close to the value for the niobium filter of 22%. The reduction in H_E with the copper filter is 7% less than that obtained with the niobium filter. These results are in disagreement with the conclusions of Nagel (1989), based on computer simulations. He claimed that both real K-edge filters and pseudo K-edge filters such as yttrium, niobium and molybdenum are by no means superior to ordinary copper filters. In the case of chest radiography, considered in this work, the dose reduction effect of the copper filter can probably be intensified by increasing the filter thickness and can perhaps be brought to the level of the niobium filter. However, this higher filtration will certainly require a strong increase in tube load, significantly exceeding that required for the niobium filter.

Conclusion

Our study shows that for a heterogeneous patient population, the addition of a 50 μm thick niobium filter to the usual filtration of 2.5 mm aluminium results in a decrease in the effective dose equivalent of 17% for a PA chest X-ray examination. Adopting the radiation risk estimate of 125×10^{-4} per Sv from ICRP (1977), the risk for fatal cancer is reduced by 0.19 cases per million examinations using the niobium filter.

The reduction in the effective dose equivalent using the copper filter with equivalent thickness (0.15 mm, using the equal HVL for aluminium criterion) is only 10%. A comparison shows that the performance characteristics of the niobium filter are significantly better from the point of view of patient dose reduction. Concerning the image quality, no difference between the niobium and the copper filter could be observed.

The results confirm that drastic alterations in patient dose by the addition of a dose reduction filter to the usual filtration cannot be expected (Nagel, 1989).

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Advances in treatment planning dosimetry for a high energy neutron beam

By S. W. Blake, MSc

Physics Department, Clatterbridge Hospital, Merseyside, UK

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Abstract. Before starting the clinical programme, a series of physical measurements were made using the Clatterbridge high energy neutron facility. These consisted of measurements made under standard conditions, *e.g.* with square fields, full scatter conditions and perpendicular beam incidence. Further measurements have now been performed to include various clinically relevant non-standard conditions. These included the effects of field shape, backscatter, oblique incidence, bolus and beam blocking on dose distributions.

Since January 1986 the Clatterbridge High Energy Neutron Facility has been used to treat neoplastic disease in a variety of sites as part of a programme of clinical studies. These studies have largely taken the form of radomized clinical trials in which patients receive treatment with either neutrons or megavoltage X rays. A fuller description of the facility may be found elsewhere (Bonnett et al, 1988).

Before commencing clinical use of the machine, quantitative measurements were performed to enable treatment planning and delivery of patient doses (Shaw et al, 1988). Most of these measurements were performed under a limited set of standard physical conditions, *e.g.* with square fields, full scatter conditions and perpendicular beam incidence. In the clinical situation these are seldom met, and corrections are necessary for the non-standard geometry in which patients are irradiated. The purpose of this paper is to present the results of investigations into field shape, backscatter, oblique incidence, bolus materials, beam blocking and dose transition effects.

Method

Equipment

An Exradin 0.5 cm^3 tissue equivalent (TE) ionization chamber continuously flushed with methane based TE gas was used to determine total absorbed dose (neutron plus γ) for the majority of the measurements. A water filled phantom with dimensions 50 cm × 50 cm × 50 cm was used for the measurements requiring full scatter contribution. Unless otherwise stated, the phantom surface was placed at the isocentre, 150 cm from the target. For the measurements of dose distributions in the presence of beam blocks, a Far West Technology 0.1 cm^3 TE chamber flushed with TE gas was used. A thin window parallel plate ionization chamber with a 5 μm thick aluminized Mylar window was used for the transition zone dosimetry.

Field shape effects

Preliminary measurements have shown that the effects of field shape on output factor and percentage depth dose could be accounted for by the use of an equivalent square (EQS) relationship of the form:

$$\mathrm{EQS} = \frac{2\mathrm{AB}}{(\mathrm{A}+\mathrm{B})}$$

and for wedge factor a relationship of the form:

$$\mathrm{EQS} = (\mathrm{AB})^{0.5}$$

The limitations of these relationships were assessed by performing a series of measurements of these parameters for nominally equivalent square and rectangular fields related using the relevant formulae.

Absorbed dose per monitor unit (output) was determined on the central axis of a field at the dose maximum.

Depth dose was investigated by determining the depth of the 50% central axis dose level from measurements either side of this value. Wedge factors were measured at dose maximum on the beam central axis. The extension of the above relationships to simple irregular fields was investigated by performing measurements both with and without the presence of a beam block, and also by performing measurements with equivalent square fields. For these measurements the terms AB and A + B were taken to represent the field area and half the perimeter respectively, *e.g.* a 2 cm × 2 cm block in the corner of a 10 cm × 10 cm field will not change the perimeter of the beam, but the area will change by 4%. The beam block was positioned approximately 30 cm from the phantom surface.

Effect of SSD on wedge factor. When patients are treated isocentrically, a given field size is equal to the

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Present address: Medical Physics Department, Royal Devon and Exeter Hospital, Exeter, Devon, UK.

collimator setting at the isocentre but reduced by a geometrical factor at the surface. If the wedge factor (measured at the isocentre) varies significantly with field size, then it has to be decided whether to use the surface or isocentric field size for calculation of clinical wedge factors (WFs). This was investigated by determining the WF for a certain field size at 150 cm source–skin distance (SSD), and then reducing the SSD to 130 cm. The WF was then re-measured without adjusting the collimator. The collimator was then adjusted to give the original field size at the phantom surface, and the WF measured again. In this way the ratio of the WF at 150 cm to that at 130 cm could be determined for the two alternative ways of specifying field size.

Backscatter

The effect of missing backscatter on the exit surface was determined using the "half immersed chamber" technique (Légaré, 1964). This was accomplished by directing the beam vertically upward, and irradiating through the base of the phantom (see Fig. 1). The phantom was filled to the required level, and the chamber positioned at this depth. The thickness of backscatter was then varied by filling the phantom beyond this level. Measurements were made for field sizes of 5 cm × 5 cm, 10 cm × 10 cm, and 20 cm × 20 cm with the backscatter thickness ranging from 0.1 to 10 cm, at depths of 5, 10 and 20 cm. Subsequently, measurements were made at 2 cm deep for a 10 cm × 10 cm field with and without a 5 cm thick Polythene filter over the end of the collimator. This was to ascertain whether low energy neutrons contributed to the backscatter effect.

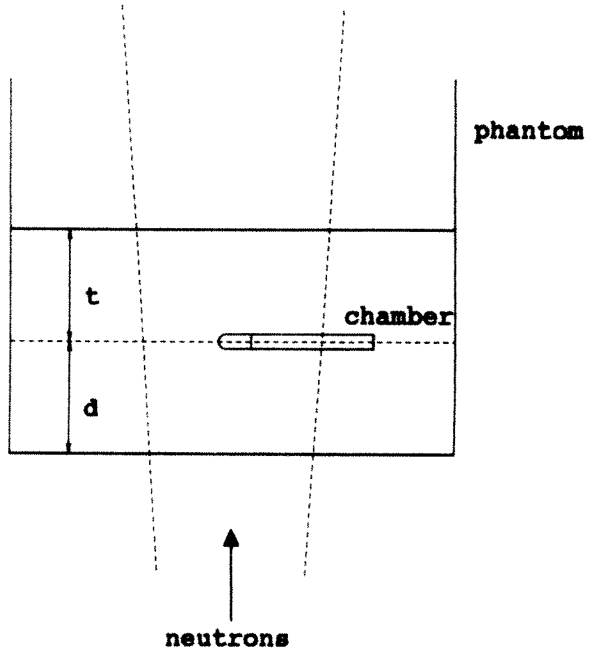


Figure 1. Irradiation geometry for the backscatter measurements. The chamber was positioned at various depths (d) and the thickness of backscatter (t) was then varied.

Oblique incidence

The effect of oblique incidence on a dose distribution was investigated by positioning a water filled phantom with its front surface at an angle of 45° to the beam direction. Measurements were made at selected points in the phantom (see Table I) for comparison with the prediction of the IGE RT/PLAN treatment planning system, which uses the effective SSD method for oblique incidence correction (ICRU, 1976).

Bolus materials: attenuation and dose transition effects

A tissue substitute material with the same hydrogen concentration as ICRU muscle tissue was produced using a mixture of 44.2% paraffin wax and 55.8% icing sugar by weight. This resulted in an elemental composition of 10.2% hydrogen, 61.1% carbon and 28.7% oxygen, and a density of 1.19 ± 0.02 g/cm^3. The aim of this was to produce a material with a kerma per unit neutron fluence close to that of tissue, for use as a bolusing material. The attenuation characteristics of the wax–sugar mixture were studied by positioning an Exradin ionization chamber 10 cm deep in a water phantom, and irradiating with a 10 cm × 10 cm field. Blocks of the material were added on the inside face of the phantom (Fig. 2), to highlight the *difference* between water and the bolus material as a function of thickness.

The thin window ionization chamber was placed beneath samples of the bolusing materials, and irradiated from above. For these measurements the height was adjusted so that the bolus surface was kept at the isocentre. Readings were taken relative to those obtained with a sample of A150 plastic irradiated under the same geometry. This experimental set-up was used to determine the thickness of build-up material required to produce a dose rate at the skin surface equal to that at the dose maximum, *i.e.* effectively to shift the dose maximum to the surface. Measurements were also made

Table I. Comparison of measured (M) and predicted (P) doses for a beam incident at 45° to the phantom surface

Depth (cm)	−3 cm off axis		Central axis		+3 cm off axis	
	M	P	M	P	M	P
5	82%	83%	90%	90%		
10	62%	63%	70%	71%	83%	80%
15	47%	47%	53%	54%	62%	60%

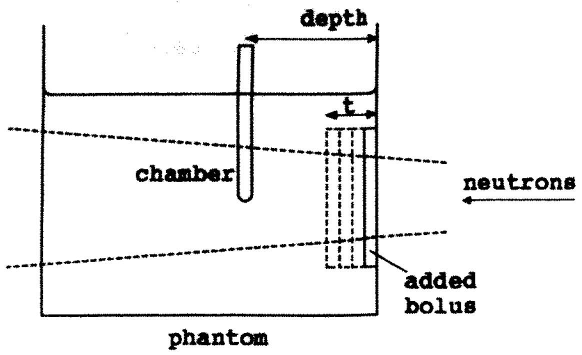


Figure 2. Irradiation geometry for the determination of the difference in attenuation between bolus materials and water.

to investigate the effect of a layer of Cabelite (cellulose acetate butyrate) between a layer of wax bolus and the patient. Cabelite is the material from which the patient treatment shells are made. The effect of a layer of lead between bolus and skin surface was investigated as a means of *reducing* skin dose. This was performed by interposing varying thicknesses of lead foil between a block of A150 plastic and the front window of the ionization chamber.

Beam blocks

Field shaping for the Clatterbridge neutron beam is accomplished using 12 cm thick beam blocks attached to the accessory ring. The blocks are manufactured from a tungsten alloy with the composition 95% tungsten, 3.5% nickel and 1.5% iron.

Narrow beam measurements were made to assess the attenuation by the blocks. A field size of 5 cm × 5 cm was used, with the blocks positioned at the end of the collimator. An ionization chamber with an 18 mm thick build-up cap was positioned "free in air" at the isocentre.

For the beam scans used to produce isodose curves, blocks were positioned on the accessory ring, and the field was scanned under computer control.

Results

The uncertainties quoted with the results in this paper represent one standard deviation. Error bars are shown on the graphs when they are larger than the symbols used.

Field shape effects

Output. The output was measured for field sizes ranging from 16 cm × 7.3 cm to 30 cm × 10.9 cm with equivalent squares of 10 cm and 16 cm respectively. It was found to be independent of field elongation to within ±1% for any given equivalent square. The effects on output of irregular fields produced by beam blocking were to produce an *increase* in dose of approximately 0.5% for beam blocks covering up to 30% of the field area. A subsequent measurement, with the phantom moved 15 cm closer to the target, showed a larger increase in output of 1.1±0.2%.

Depth dose. The depths of the 50% isodose levels for

Table II. Variation of depth of 50% dose with field shape
(a) Rectangular fields (*A* is wedged field axis)

Field size (cm) *A* × *B*	Wedge	Eqs (cm)	Elongation *A*/*B*	Depth of 50% (cm)	Difference (cm)
10 × 10	0	10	1	16.1±0.1	
14 × 7.8	0	10	1.79	16.1±0.1	0
16 × 7.3	0	10	2.19	16.0±0.1	0.1
16 × 16	0	16	1	18.1±0.1	
25 × 11.8	0	16	2.12	18.0±0.1	0.1
30 × 10.9	0	16	2.75	17.9±0.1	0.2
10 × 10	2	10	1	16.5±0.1	
7.3 × 16	2	10	0.46	16.5±0.1	0
16 × 7.3	2	10	2.19	16.4±0.1	0.1
16 × 16	2	16	1	18.3±0.1	
10.9 × 30	2	16	0.36	18.2±0.1	0.1
30 × 10.9	2	16	2.75	18.4±0.1	0.2

(b) Irregular fields

Field size (cm) *A* × *B*	Block size (cm) *A* × *B*	EQS (cm)	Depth of 50% (cm)	Difference (cm)
8.2 × 8.2		8.2	15.5±0.1	
10 × 10	3 × 10	8.2	15.3±0.1	0.2
8.4 × 8.4		8.4	15.7±0.1	
10 × 10	4 × 4	8.4	15.6±0.1	0.1

Table III. Wedge factor variation for rectangular fields

Field size[a] (FS) (cm)	Wedge no.	Equivalent square (EQS)	WF(FS)/WF(EQS)
20 × 12.8	1	16	1.011 ± 0.005
12.8 × 20	1	16	1.010 ± 0.005
6.3 × 16	2	10	0.994 ± 0.005
16 × 6.3	2	10	1.005 ± 0.005
8.5 × 30	2	16	1.021 ± 0.005
30 × 8.5	2	16	1.021 ± 0.005
12.8 × 20	2	16	1.001 ± 0.005
20 × 12.8	2	16	1.003 ± 0.005
6.3 × 16	3	10	1.003 ± 0.005
16 × 6.3	3	10	1.007 ± 0.005
8.5 × 30	3	16	1.015 ± 0.005

[a] Wedged field dimension given first.

Table IV. WF measured at 130 cm/WF measured at 150 cm for (a) constant surface field size or (b) constant collimator setting

Field size at 150 cm	Wedge no.	(a) Constant field size	(b) Constant collimator setting
10 × 10	1	0.983 ± 0.005	0.995 ± 0.005
10 × 10	2	0.983 ± 0.005	0.998 ± 0.005
11.5 × 11.5	2	0.978 ± 0.005	0.995 ± 0.005
16 × 16	2	0.978 ± 0.005	0.993 ± 0.005
20 × 20	2	0.977 ± 0.005	0.987 ± 0.005
5 × 5	3	0.986 ± 0.005	0.989 ± 0.005
10 × 10	3	0.980 ± 0.005	0.998 ± 0.005
	Means:	0.981 ± 0.003	0.994 ± 0.004

a range of fields related using the equivalent square formula are presented in Table II. Good agreement was obtained over the range of field sizes and shapes investigated. The small random variations in the depth of the 50% value are within the limits of experimental uncertainty.

Wedge factors. The results are presented in Table III in the form WF_{rect}/WF_{square} for a variety of field size and wedge combinations. A possible trend is shown in that the ratio deviates from unity with increasing elongation.

Effect of SSD on wedge factor. The ratios of WFs measured at 130 cm SSD to those measured at 150 cm are displayed in Table IV. It can be clearly seen that there is better agreement (ratio closer to unity) for constant collimator setting rather than constant surface field size. If WFs are taken from the *surface* field size when using short SSD, errors of 1–2% could result. The use of collimator setting (equal to surface field size at the *isocentre*) enables the use of values determined at 150 cm SSD with an uncertainty of 0.5%.

Backscatter

The results are plotted in Fig. 3 in which the doses are normalized to a backscatter thickness of 10 cm. The effect of missing backscatter is enhanced for larger field sizes, and also for shallower depths. For the largest field size, the magnitude of the effect is greatest at 5 cm deep, goes through a minimum at about 10 cm deep, then again increases beyond this depth. The ratio of the dose with 1 cm backscatter to that with 10 cm is plotted as a function of depth in Fig. 4. The effect of the Polythene filter is seen as an increase in this ratio at shallower depths.

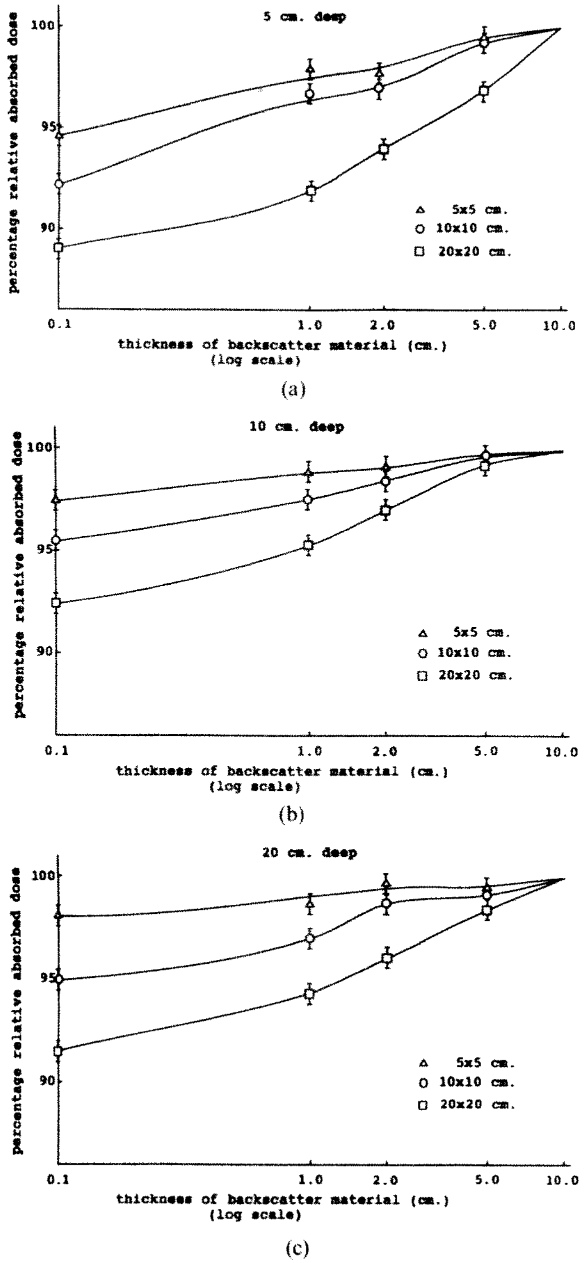


Figure 3. Absorbed dose at (a) 5 cm, (b) 10 cm and (c) 20 cm deep relative to that obtained with 10 cm backscatter *versus* thickness of backscatter.

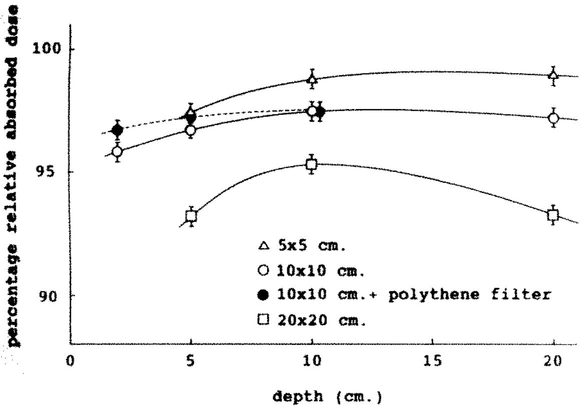


Figure 4. Absorbed dose with 1 cm backscatter relative to that with 10 cm backscatter for various field sizes *versus* depth. The effect of a Polythene filter is shown by the dotted line.

Oblique incidence

The results are presented in Table I. The maximum difference between the measured and predicted values is 3%, with most of the the differences within 2%.

Bolusing materials: attenuation and dose transition effects

Attenuation effects. The *difference* between water and the bolus material is shown in Fig. 5. It was found that 5 cm of the material reduced the dose by 3%. The same thickness of paraffin wax reduced the dose by 1.4%.

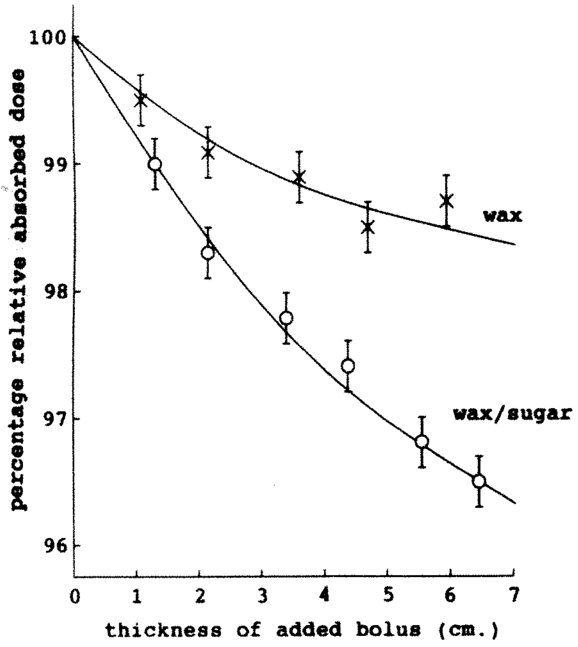


Figure 5. Absorbed dose at 10 cm deep in water *versus* the thickness of bolus material substituted for water (see Fig. 2).

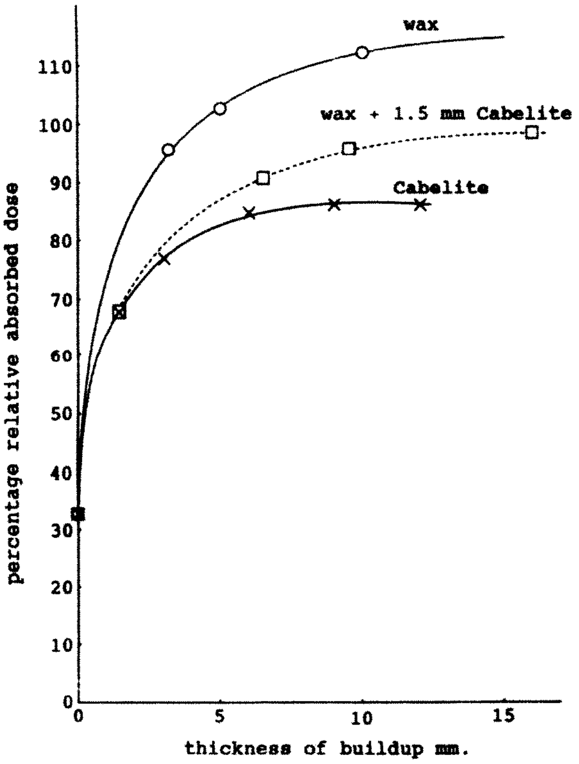


Figure 6. Absorbed dose behind wax (○) Cabelite (×) and wax in front of 1.5 mm Cabelite (□) *versus* thickness of the materials.

Dose transition effects. The dose adjacent to the sample of wax–sugar mixture was within 3% of the dose adjacent to A150 plastic, but for wax alone the dose was 15% higher. This indicates that full build-up may be obtained with a reduced thickness of wax. Dose transition curves for wax, Cabelite and wax attached to Cabelite (with Cabelite next to the chamber) are given in Fig. 6. Full dose build-up occurs for approximately 4 mm of wax alone, and 15 mm of wax attached to 1.5 mm of Cabelite. Full dose build-up is not attained in Cabelite alone because of the lower kerma in this material.

Restoration of skin sparing. The result is shown in Fig. 7. Almost full sparing is restored with a thickness of 2 mm, and only 0.5 mm reduces the dose to 58% of the value with no lead present.

Beam blocks

The results from the narrow beam attenuation measurements were found to be well fitted by a single exponential function. The half-value thickness was found to be 2.69±0.08 cm, and for a 12 cm thick block the transmission is approximately 5%.

A set of beam profiles measured in the presence of a block is shown in Fig. 8 and the resulting isodose distribution in Fig. 9(a). In the presence of the phantom, the effect of the scattered radiation is to increase the

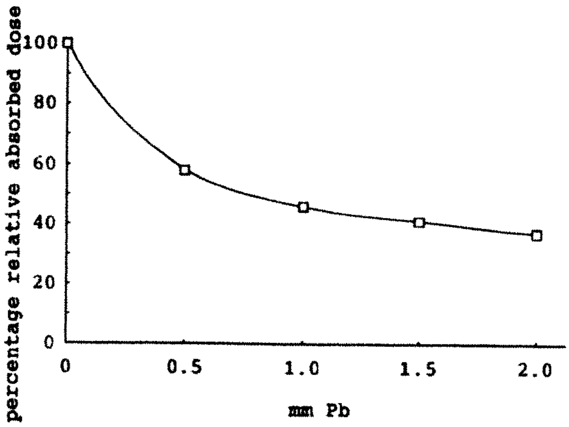


Figure 7. Absorbed dose behind A150 plastic *versus* the thickness of lead between the plastic and the chamber.

absorbed dose in the shadow of the block to approximately 20%, compared with 5% obtained under narrow beam geometry. The IGE RT/PLAN treatment planning system was used to predict the isodose distribution, corrected for the presence of a block (Fig. 9(b)).

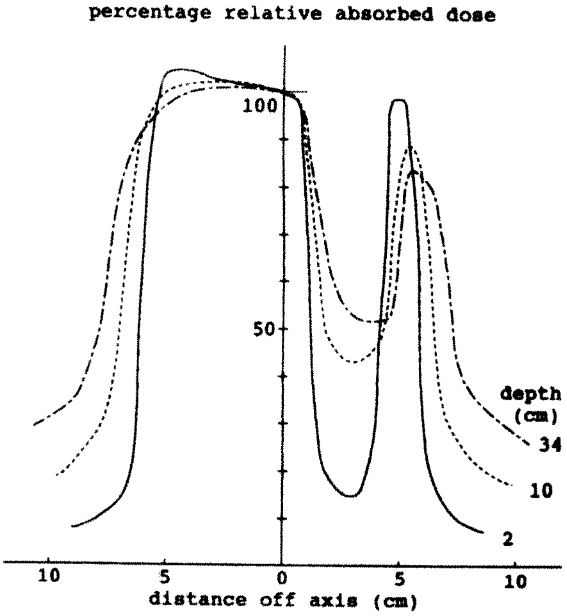
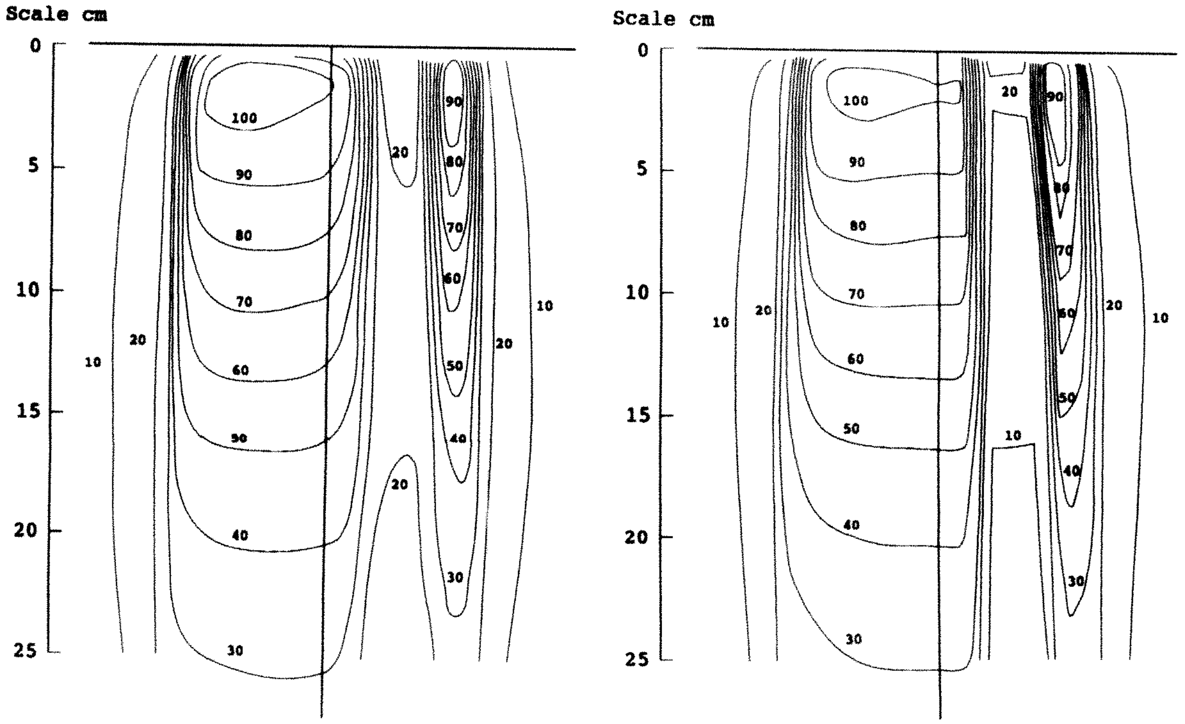


Figure 8. Profiles of absorbed dose *versus* distance off axis at 2, 10 and 34 cm deep.

Discussion

Previous measurements have shown that both the output and the depth dose of the Clatterbridge neutron beam vary more with field size than for a photon beam of similar penetrating power (Shaw et al, 1988), stressing the need for an accurate means of calculating the effective field size for rectangular and irregular fields. The



(a)

(b)

Figure 9. Isodose curves in the presence of a beam block, (a) measured and (b) predicted using RTPLAN.

same set of measurements also showed that the use of the equivalent square formula as defined above resulted in incorrect WFs for rectangular fields. Wedge factors for rectangular fields were found to be more accurately fitted to square field data by specifying WFs for the same *field area*.

The variation in output factor with field shape for rectangular fields produced using the collimator alone is well accounted for using the equivalent square relationship EQS = 2AB/(A + B). This is in agreement with the findings of a similar investigation for a lower energy neutron beam (Williams et al, 1979). The results for irregular fields produced using beam blocks were anomalous in that their effect was to *increase* output slightly. This is considered to result from scatter from the block, and the subsequent measurements with the phantom closer to the target gave support to this hypothesis. Decreases in output of up to 5% would be expected if the field area were reduced by a similar amount using the collimator alone.

The same equivalent square relationship provides a good fit to the data for depth dose, for both rectangular *and* irregular fields. This is in agreement with previously reported measurements in a neutron beam of similar energy (Rosenberg & Awschalom, 1981). For a fuller discussion of equivalent square effects the reader is referred elsewhere (BIR–HPA, 1983).

The equivalent square relationship for wedge factor, EQS = $(AB)^{0.5}$, provides a reasonable fit to the data over the range of field sizes investigated. For the most elongated fields the agreement was within 2%, with the suggestion of a trend towards reduced quality of fit with increased elongation. The measurements of wedge factors at different SSDs indicate that factors measured at one SSD can be applied to others, provided field size is defined *isocentrically*. For example, the same wedge factor for a 10 cm × 10 cm field at 150 cm SSD can be applied when the SSD is reduced to 130 cm, where the *surface* field size becomes 8.7 cm × 8.7 cm.

The backscatter results are in agreement with similar measurements in a P(66)Be(49) neutron beam (Awschalom et al, 1982), and suggest a dependence of backscatter on depth which has not been reported in similar studies with megavoltage photon beams (Lambert et al, 1983). The *increased* effect at shallower depths is more characteristic of orthovoltage radiation (Légaré, 1964). It can be clearly seen that reductions in the *exit* dose of greater than 5% could occur for irradiations of head and neck tumours with fields greater than 10 cm × 10 cm. For most clinical situations in which backscatter could be significant (*e.g.* head and neck cancer), the points of interest lie at depths greater than the dose maximum. Thus for parallel opposed field irradiations, the dose maximum of one field becomes the point at which dose is reduced owing to lack of backscatter from the other. To define a "clinically significant" measure of backscatter, the ratio of absorbed dose with 1 cm backscatter to that with 10 cm is plotted in Fig. 4. It was postulated that the increased backscatter effects at shallow depths could be due to the presence of significant numbers of neutrons at the low energy end of the spectrum. Measurements made with a 5 cm thick Polythene filter over the end of the collimator to attenuate preferentially any low energy neutrons are included in Fig. 4. The effect of missing backscatter is greatest at 2 cm deep, and the Polythene filter is shown to be effective in reducing the magnitude of the effect. These findings support the low energy neutron hypothesis, which has also been postulated to explain physical, and biological effects observed in the Clatterbridge neutron beam (Hornsey et al, 1988; Blake et al, 1990). Neutron spectral studies (Crout et al, 1988) also showed a hardening effect with depth. Beams which have been modified by the deliberate introduction of a Polythene hardening filter should not display such marked backscatter effects. However, hardening of the beam does not explain the anomalous *increase* in the effect of backscatter beyond 10 cm deep, and for larger field sizes. This is likely to be due to the build-up of scattered radiation within the phantom.

The computer algorithm that corrects for oblique incidence is based on the effective SSD model (ICRU, 1976). The agreement between the predictions of this model and the measured data is satisfactory considering the experimental error and the limitations of the model. This result is in agreement with measurements performed on other low and high energy neutron beams (Rassow & Hensley, 1981; Vynckier et al, 1981). A model based on the addition of primary and scattered components may provide a better fit to the data.

Bulk attenuation and dose transition effects associated with the use of "bolusing" or "build-up" materials are important in that they may lead to overdosage or underdosage of a particular tissue. For neutrons, effects similar to those of megavoltage photons are observed, with differences arising from variations in kerma and secondary charged particle spectrum. The dosimetry of neutron beams is complicated by the fact that absorbed dose is specified in ICRU muscle tissue (ICRU, 1977), and that for *relative* dose distribution measurements the phantom material is water (Mijnheer et al, 1987). Solid phantom materials having the same elemental composition as ICRU muscle tissue are not available, and the substitution of some components for others is inevitable. For this reason it is necessary to apply a kerma correction factor between A150 plastic (of which TE ionization chambers are constructed) and ICRU muscle tissue. The difference between any tissue substitute material and water is also evident in the differences in their bulk attenuation properties (Awschalom et al, 1983). These effects are evident for the two bolus materials under consideration. Although the dose behind a sample of the wax–sugar mixture was within 3% of that behind A150 plastic, 5 cm of the material reduced the dose 10 cm deep by 3%, which corresponds to an *effective* density for the material of 1.12 ± 0.02 g/cm^3. For the wax alone, the same thickness reduced the dose by 1.4%. However, the use of wax bolus could result in a 15% overdose to the skin, unless the thickness is reduced to 0.5 cm, or another material is placed between the skin and bolus. An example of this latter case is the use of wax build-up on the surface of a treatment shell. The effect of 1.5 mm of Cabelite is clearly seen to reduce the dose in the presence of wax.

A layer of lead between bolus and the skin surface as a means of *reducing* the skin dose, *i.e. restoring skin sparing*, has been used elsewhere (Bewley, 1989). For this beam, only 0.5 mm of lead is required to almost halve the surface dose behind bolus. The method is effective because kerma in lead is significantly lower than in tissue, and the secondary charged particles from the bolus are readily stopped by a layer of high atomic number material. The net result of this is that compensation for missing tissue is possible for neutrons using lead lined bolus, without the problems associated with the use of bolus for megavoltage photons. Hence, compensators positioned remotely from the patient are seldom or even never required. It should be noted that the relative biological effectiveness (RBE) of the radiation in a transition zone may not be the same as under conditions of charged particle equilibrium. Radiobiological measurements using monolayers of adherent cells to provide the spatial resolution (*e.g.* Barendsen & Beusker, 1960) are needed to investigate these effects.

It is clear that the dose in the shadow of a beam block is made up of primary and scattered radiation, and that in the example shown, scatter is the dominant contribution. Because of this, beam blocking will be most effective at the surface, becoming less so with increasing depth. This is similar to the situation near the geometrical edge of the beam, except that the transmitted component is greater. The IGE RT/PLAN model takes no account of scatter, so the "transmission" had to be set to a value of 20% in order to provide a reasonable fit to the data. The *effective* transmission through any beam block will therefore depend on the size of the block and the position of the point of interest. In critical situations *in vivo* dosimetry should be used to check beam block effectiveness (Blake et al, 1990).

Conclusions

The equivalent square relationship is valid for the determination of output and percentage depth dose for rectangular fields. When beam blocks are used, the output is not significantly different from that of the unblocked field. However, irregular fields produced using beam blocks *do* change the percentage depth dose, and a good approximation to the equivalent square under these conditions is given by 4 × area/perimeter.

For wedge factors, the size of the square field having the same factor as a rectangular field is given by the square root of the field area. For SSDs less than 150 cm, the field size at 150 cm (*i.e.* the isocentre) should be used.

The effect of missing backscatter is more significant with increasing field size and decreasing depth. Care should be taken that lack of backscatter does not produce underdosage of tumours. The oblique incidence correction used in the IGE RT/PLAN treatment planning system is of adequate accuracy when used for high energy neutrons.

Paraffin wax may be used as a bolusing material, provided it is placed on the outside of a treatment shell, or lined with lead to absorb the secondary charged particles. For use as build-up, approximately 5 mm is needed to give 100% skin dose. Alternatively, the wax–sugar mixture is suitable provided that no problems are caused by the greater attenuation of this substance than water.

Beam blocking is not as effective for neutrons as it is for megavoltage photon beams. This is because of a more significant scatter component within the patient.

The dosimetry of any new radiation modality is of considerable importance if accurate dose–effect relationships are to be established. The results presented in this paper have highlighted areas in which the physical characteristics of a high energy neutron beam require careful consideration with regard to treatment planning.

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Combined tissue oxygen tension measurement and positron emission tomography studies on glucose utilization in oncogene-transformed cell line tumour xenografts in nude mice

By *F. Kallinowski, PhD, A.-L. Brownell, PhD, †P. Vaupel, MD, PhD and G. L. Brownell, PhD

Physics Research Laboratory, Massachusetts General Hospital, Boston, MA 02114, USA, *Department of Surgery, University of Heidelberg, D-6900 Heidelberg and †Institute of Physiology and Pathophysiology, University of Mainz, D-6500 Mainz, Germany

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Abstract. Glucose utilization studies using high resolution positron emission tomography and tissue oxygenation measurements using microelectrode techniques were carried out in nude mice bearing oncogene-transformed (Rat1pEJ6.6 and REFpneoMYCrasEpool) cell line tumours and a non-transformed (Rat1) cell line tumour to determine the correlation between glucose utilization, tissue oxygenation and tumour growth rate. Control measurements were performed in the subcutis of tumour-free animals. Accelerated growth rates were observed in both ras-transformed cell lines with tumour doubling times of 2.5–4 days while Rat1 tumours had a doubling time of 28 days. Since rapid growth rates necessitate elevated consumption of oxygen and nutrients, severe tumour hypoxia was observed in tumours from both ras-transformed cell lines; median pO_2 being 1–5 mmHg (tumour sizes ca. 400 mm^3). Size-matched Rat1 tumours exhibited a median pO_2 value of 12 mmHg corresponding to the slow growth rate. Comparing both ras-transformed cell lines, Rat1pEJ6.6 tumours had a more adequate vascularization than REFpneoMYCrasEpool tumours indicated by a better tissue oxygenation (5 mmHg *versus* 1 mmHg) and higher glucose metabolic rates (13.4 ± 2.2 μmol/min/100 cm^3 *versus* 9.7 ± 1.3 μmol/min/100 cm^3). At advanced growth stages, a reduction of tissue oxygen levels is obtained which is accompanied by a 30% elevation of glucose metabolic rate. The data presented here demonstrate for the first time an impact of well defined oncogenic alterations on the therapeutically relevant parameters of the micromilieu of malignant tumours.

Research on oncogenesis is one of the most active areas of biological research in current years. Most of this work to date has been molecular in focus, and very little is known about the *in vivo* phenotypes obtained when these malignant cells are actually grown in animal hosts. A preliminary study (Kallinowski et al, 1990) indicated that therapeutically relevant alterations of the metabolic microenvironment in solid tumours are observed after oncogenic transformation.

Recently, the development of high resolution positron emission tomography (HR-PET, Brownell et al, 1985) has made it possible to study very small tumours in laboratory animals. For the first time, it is possible to determine phenotypic effects of oncogenes with a very high degree of sensitivity, *in vivo* and non-invasively.

Tumour metabolism provides the energy required for unrestricted proliferation. Thus, rapid cell turnover necessitates high metabolic rates. In 1931 Warburg showed that glycolysis is increased in rapidly growing tumours. In 1963, Sweeney et al further established that the glycolytic rate corresponded to the rate of tumour growth in rat hepatomas. Thus the more rapidly growing tumours have an accelerated glycolysis, while more differentiated tumours have glycolytic rates closer to that of normal tissues.

The *in vivo* measurement of glucose utilization requires a suitable glucose analogue. ^{18}F-2-fluoro-deoxy-D-glucose (2FDG) has proved to be one of the most promising of the available analogues (Phelps et al, 1979). It distributes and enters the metabolic cycle like glucose, but will be trapped in the tissue in the form of 2FDG-6-phosphate. Metabolic measurements of glucose can then be made by positron tomography using dynamic and static images.

The major goal in this study was to characterize therapeutically relevant biological properties of genetically defined tumour cells. Glucose uptake studies using high resolution positron emission tomography are compared with growth rate and tissue oxygenation data on the same cell lines. Glucose utilization studies were carried out on 16 and oxygen tension measurements on 50 mice bearing two oncogene-transformed and one non-transformed cell line tumours in the hind thigh (glucose measurements) or in the hind foot dorsum (oxygenation studies). In addition, glucose utilization studies were performed on two and oxygen tension measurements on 10 tumour-free mice.

Materials and methods

Cell lines

A total of three cell lines were included in the study. Fischer 344 rat embryo cells previously reported to be spontaneously tumorigenic were chosen as the control cell line (Rat1, Freeman et al, 1973). Rat1 cells were transfected with copies of a variant human c-Ha-ras1 proto-oncogene to determine the impact of ras transformation (Rat1pEJ6.6, Land et al, 1983). The effect of a co-operating oncogene was evaluated with cells obtained from low-passage Fischer 344 rat embryonic fibroblast-like cultures and subsequently transfected with plasmids pT24, psVvmyc and pHSG272, encoding a mutated c-Ha-ras1 gene as well, a viral myc oncogene and a neomycin-resistance gene, respectively (REFpneoMYCrasEpool, Kallinowski et al, 1990).

The cell lines were serially passaged in conventional culture media (Dulbecco's minimal essential medium, glucose 1 g/l, Sigma, St Louis, MO, USA; 10% fetal calf serum, JR Scientific, Woodland, CA, USA; penicillin 50 U/ml, streptomycin 50 μg/ml, neomycin 100 μg/ml, Sigma, St Louis, MO, USA; 5% CO_2 and air). The cultures were split 1 : 40 once to twice a week. Exponentially growing cells from the 10th to 15th passage were harvested by trypsinization at 37°C for 5–10 min (0.05% trypsin, 0.53 mM EDTA, Gibco Laboratories, Grand Island, NY, USA).

Tumours grew subcutaneously in the dorsum of the hind foot of 8-week-old nude mice after the injection of approximately 10^6 cells. The mice were bred and maintained in a defined flora colony (Sedlacek & Mason, 1977) and received 6 Gy (600 rad) whole-body irradiation about 24 hours prior to tumour implantation. In order to assess volume doubling times, serial caliper measurements of three orthogonal diameters were performed and tumour volumes were calculated as a rotation ellipsoid (Steel, 1977).

Studies with pO_2

The measurement system originally described by Weiss and Fleckenstein (1986) was recently applied to oxygen measurements in animal tumours (Vaupel et al, 1989a). Needle electrodes with a steel shaft of 330 μm outer diameter contained a gold disc with a radius of 6 μm recessed within a teflon filling of 20 μm. The system further consisted of an amplifier unit which provided the polarization voltage of −700 mV (against a Ag/AgCl reference electrode), controlled the electrode movement and performed the data evaluation (KIMOC 6650, Eppendorf, Hamburg, FRG). Before each tissue measurement the electrodes were calibrated in 0.9% saline equilibrated with air or pure nitrogen gas ($pO_2 = 0$ mmHg). Typical electrode characteristics were oxygen sensitivities of 2–3 pA/mmHg pO_2, response times around 600 ms and drift values less than 1% between pre- and post-study calibration ($T = 37°C$). Oxygenation measurements in tissue typically took less than 5 minutes. An electrode was inserted through a skin incision (< 1 mm) and initially advanced about 1 mm. After an equilibrium period of < 2 minutes, the electrode was moved through the tissue with a step length of 1 mm. In order to minimize tissue compression the electrode was immediately withdrawn by 0.3 mm after each forward movement. Data were obtained at each position within 1.4 seconds. A total of 20–60 values were obtained in each tumour and, as a control, in the subcutis of the hind foot dorsum. Ten tumours were measured on each of the three different cell lines. In addition 10 tumours were measured in each size group (71 ± 4, 407 ± 9 and 716 ± 45 mm^3) to follow changes during tumour growth. For the computation of local tissue pO_2 values, temperature differences between the calibration vessel, tumours and subcutis were taken into account. To assess differences between the various tissues, frequency distributions were compiled from these data. The histograms obtained were characterized by median pO_2 values and 10th and 90th percentiles.

HR-PET studies

Animal preparation. To image glucose utilization using positron emission tomography, a small catheter (PE-10 tubing, Clay Adams, Boston, MA, USA) was placed into the carotid artery or jugular vein of the anaesthetized mouse (pentobarbital, 0.05 mg/g intraperitoneally) for the administration of 2FDG [3.7–8.9 MBq (100–240 μCi) in 0.1–0.2 ml]. In two normal mice, catheters were placed into both the carotid artery and jugular vein. The venous line was used for administration of activity and the arterial line for serial blood sampling. Rectal temperature of the animals was followed throughout the experiments. Mean rectal temperature of anaesthetized animals used in PET studies was 36.6 ± 0.2°C, the rectal temperature of 10 conscious, restrained nude mice being 36.6 ± 0.1°C.

Synthesis of ^{18}F-2-deoxy-D-glucose (2FDG). ^{18}F-2-deoxy-D-glucose (2FDG) was prepared by a modified method of a nucleophilic substitution technique of Hamacher et al (1986) (Korpela et al, 1988). To increase specific activity, the eluated 2FDG from the retardation column was concentrated 10 times using a rotation vaporizer. 2FDG was prepared before each study.

Imaging device. An analog-coded single ring tomograph (PCR-I) was used for positron imaging (Brownell et al, 1985). The analog ring design offers a number of advantages for positron tomography. The first is that high resolution tomographs can be obtained without sacrificing sensitivity. The analog ring design does not use absorbing masks or intercrystal shielding and is not limited by the necessity of rejecting events scattered into adjacent detector elements. A second advantage is that high resolution can be obtained without mechanical motion. This results from the use of thin, closely packed detector elements and permits fast dynamic imaging in an easily assembled system.

The resolution of PCR-I for a point source at the centre is 4.5 mm and the sensitivity is 46 000 counts per second for a 20 cm diameter source with concentration of 1 $\mu C/cm^3$. The overall efficiency is 64% of the theoretical maximum for a 1 cm plane thickness corresponding to the 2 cm high detectors. A plane thickness of 5 mm used in this study is obtained by the use of cylindrical collimators limiting the effective height of the detectors. The resolving time of PCR-I is 6 nsec (FWHM).

Imaging protocol. To measure dynamic activity curves, the anaesthetized mouse was placed in an oblique sagittal position inside the camera ring so that the heart and the tumour were in the imaging plane. 2FDG (3.7–8.9 MBq (100–240 μCi) in 0.1–0.2 ml) was administered as a bolus injection and serial images were collected every 30 seconds during 20 minutes following the injection to monitor activity in the blood pool, tumour and muscle. In two normal mice, six arterial blood samples of 10–15 μl were taken at different times to determine the disappearance of activity from the blood pool. In four tumour-bearing mice, one arterial sample was taken after imaging to calibrate the *in vivo* measured activity curve. After imaging, the arterial glucose level was determined enzymatically.

After dynamic data collection, transverse section imaging was performed slice by slice over the tumour area utilizing a computer controlled imaging table. The thickness of the slice was 5 mm and the distance between slices was 2 or 3 mm. The data were corrected for sensitivity and attenuation and image reconstruction was performed using a Hanning filtered convolution backprojection (Chesler, 1972; Stearns et al, 1987).

The calibration of the tomograph, needed for quantitation, was made using a ^{68}Ga-phantom. A cylinder of 30 mm diameter was filled with activity (concentration 5 μCi/ml) and serial images were collected for 2 hours to determine the calibration coefficient between activity and counts. Reconstruction of calibration images was performed in the same way as reconstruction of animal data.

Regions of interest with a diameter of 3 mm, corresponding to 14 pixels in the image area were selected within the ventricles of the heart to obtain blood activity. Several areas with the same size as in the blood pool were selected over the tumour and contralateral healthy thigh. The data were corrected for recovery effects (Hoffman et al, 1979) (using the value of 0.15 for recovery coefficient), the calibration coefficient and the injected activity. Recovery effect is a characteristic property for each imaging device and it depends on the resolution of the device and the size of the object to be studied. Recovery coefficient corrects the apparent isotope concentration to the true concentration. Two exponential functions were fitted to the blood activity data using a modified Marquard fitting for non-linear data (Correia et al, 1978). In two animals, these curves were compared with arterial samples to determine the accuracy of blood activity data obtained by the imaging technique. In four animals, the blood pool data were calibrated by the single arterial sample.

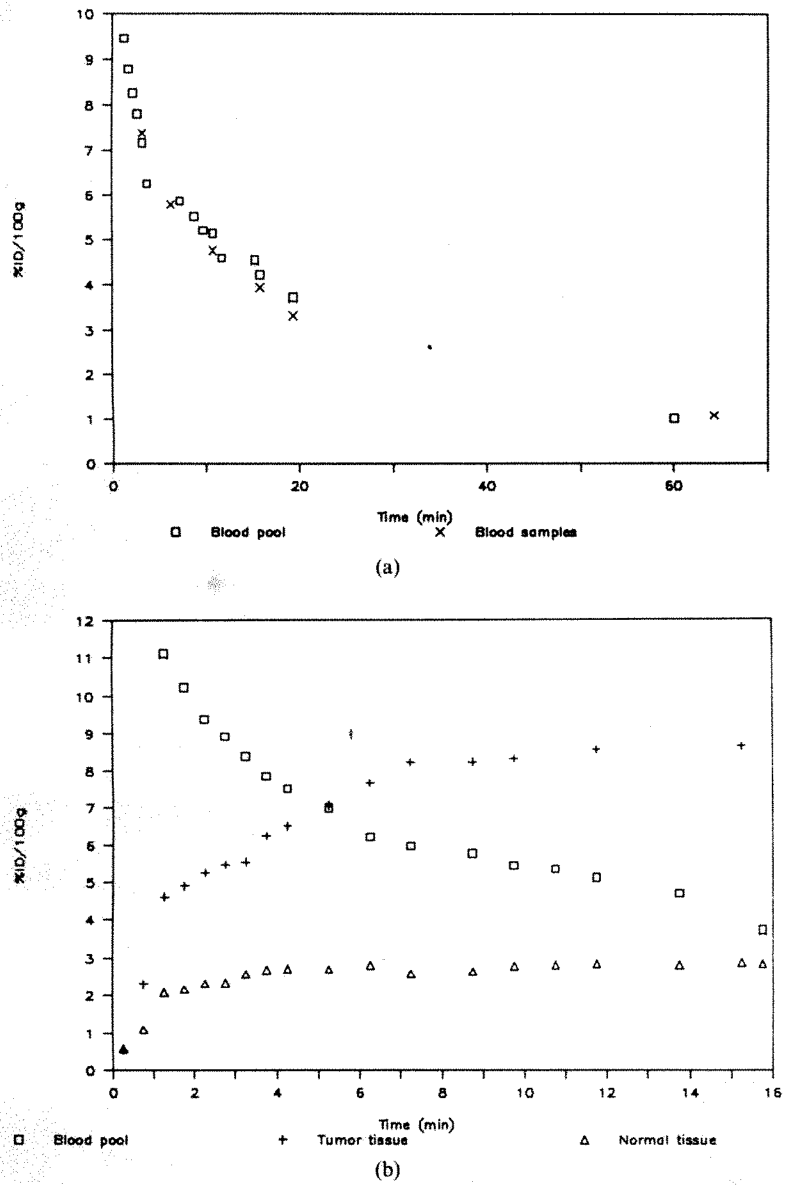
Measurement of glucose metabolic rate. ^{18}F-fluoro-2-deoxy-D-glucose distributes and enters the metabolic cycle like glucose but is trapped in the tissue in the form of 2FDG-6-phosphate, which permits metabolic measurements to be made based on positron imaging. The behaviour of 2FDG can be described by a three-compartment model (Sokoloff et al, 1977) or four-compartment model (Phelps et al, 1979). The rate constants were obtained from the measured data by means of modified Marquard non-linear fitting. A value of 0.45 was used for the lumped constant for both tumour and normal tissue. The lumped constant compares the affinity of hexokinase for glucose as opposed to deoxyglucose. By using this constant, deoxyglucose uptake in the high resolution images was converted to glucose utilization. Several small areas of interest were selected over the tumour in the quantitated images to obtain the average glucose metabolic rate.

Results

The correlation between *in vivo* measured 2FDG blood pool data and blood samples in a tumour-free mouse is presented in Fig. 1a. The regression correlation between the two curves is $r = 0.93$. The *in vivo* blood pool data were obtained from a region of interest 3 mm in diameter centred on the heart. Figure 1b shows time–activity curves in blood pool, tumour and normal tissue of a nu/nu mouse bearing a Rat1pEJ6.6 cell line tumour in a hind thigh. Figure 1b shows that the 2FDG accumulation in tumour was 4–5 times higher than in normal tissue, indicating high glucose metabolic rate in tumour. Figure 2a shows the distribution of 2FDG at different times in a nu/nu mouse bearing a Rat1pEJ6.6 cell line tumour and Fig. 2b shows transverse, coronal and sagittal slices through the mid-level of the same tumour. Figure 3a shows the distribution of 2FDG at different times in a nu/nu mouse bearing a Rat1 cell line tumour and Figure 3b shows transverse, coronal and sagittal slices through the mid-level of the same tumour. In Figs 2a and 3a it can be seen that at 1 minute after injection most of the activity is still in the blood pool and organs containing blood and only a small fraction has accumulated in the tumour. After 16 minutes the heart can be identified as a small white spot and the concentration in the tumour is dominant. Figures 2b and 3b show the activity distribution in tumour and surrounding tissues about 1 hour later.

Table I shows regional glucose metabolic rates and oxygen tensions in size matched tumours of different cell lines. Table II shows regional glucose metabolic rates and oxygen tensions in three different size groups of Rat1pEJ6.6 cell line tumour. The glucose metabolic rate in all tumours was clearly higher than in resting skeletal muscle (4.3 ± 0.8 μmol/min/100 cm^3) Rat1pEJ6.6 tumours having the highest value in size matched tumours (13.4 ± 2.2 μmol/min/100 cm^3 increasing with size up to 17.5 ± 2.1 μmol/min/100 cm^3).

Studies with pO_2 showed that, as a rule, lower oxygenation levels were detected in tumours compared with values measured in the subcutis of the hind foot dorsum of 10 tumour-free mice. In the latter, a normally distributed histogram with median pO_2 values around 47 mmHg was found with the 10th and 90th percentile being 33 and 63 mmHg, respectively (Fig. 4). By



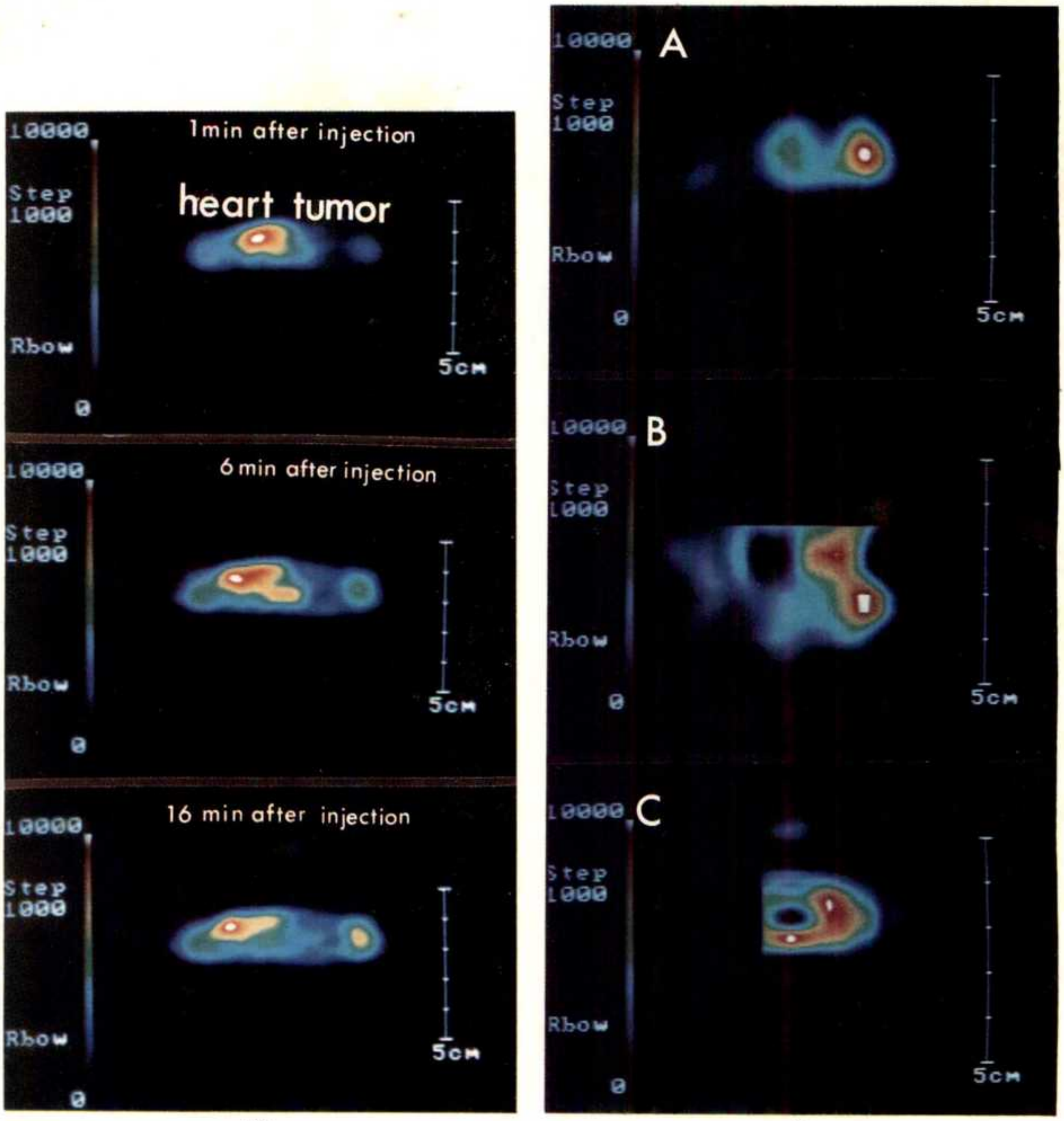
(a)

(b)

Figure 1. (a) Time–activity curves of blood pool and blood sample data in a tumour-free mouse. (b) Time–activity curves of blood pool, tumour and normal tissue of a nu/nu mouse bearing a Rat1pEJ6.6 cell line tumour in a hind thigh.

contrast, a left-shifted pO_2 histogram with a reduction of median oxygen levels and an asymmetry toward lower pO_2 values was observed in the tumours (Fig. 5).

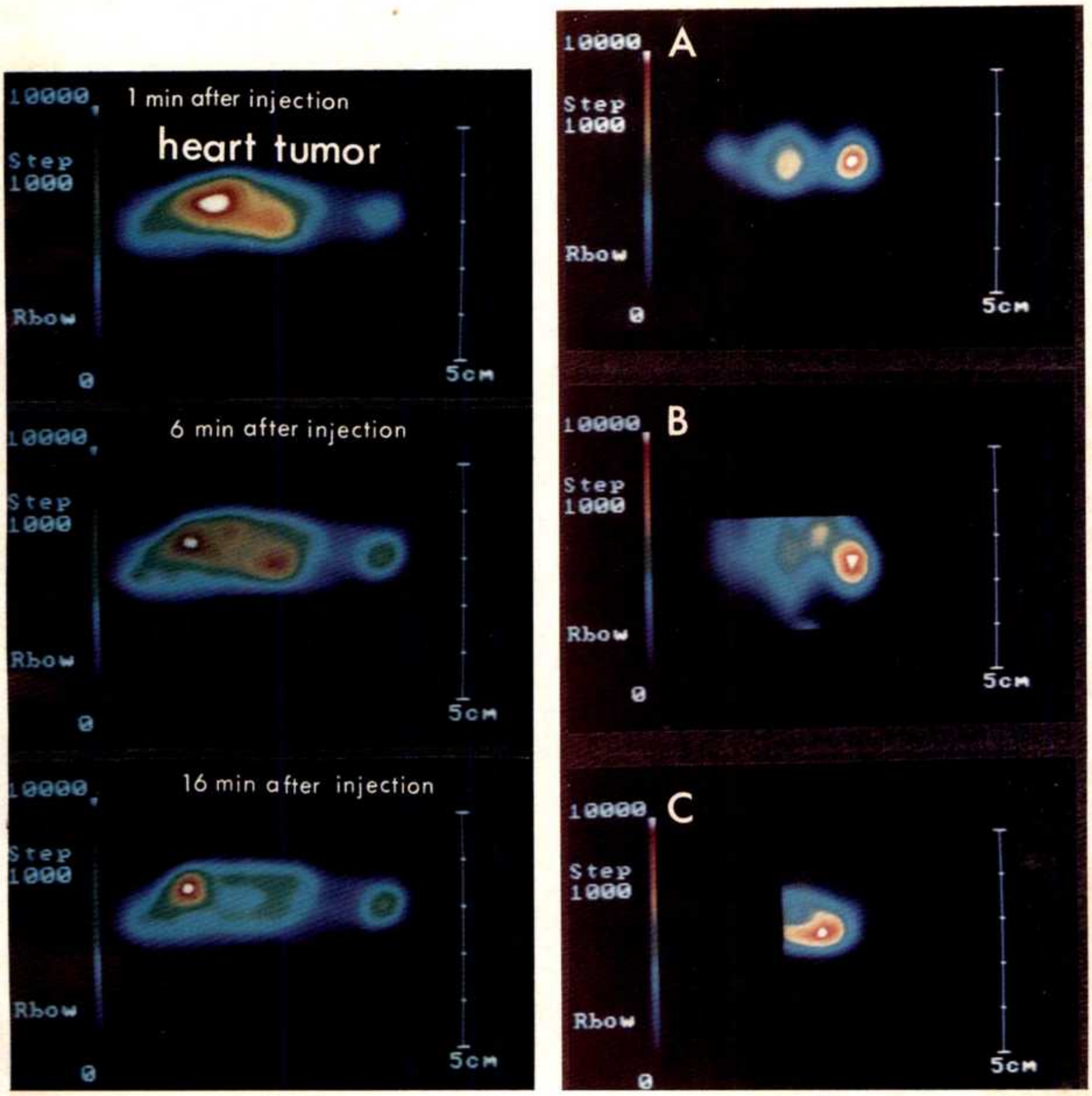
For tumour sizes comparable to those used for the PET measurements (volume around 400 mm^3), median pO_2 values of 12 mmHg were detected in spontaneously tumorigenic Rat1 tumours. Sixteen percent of all values ranged between 0 and 2.5 mmHg, *i.e.* at a level with less than half-maximum radiation sensitivity. The 10% value was at 1 mmHg and the 90% value was 33 mmHg. Rat1 tumours grew slowly with volume doubling times around 28 days. Compared with this tumour line, ras-transformed Rat1 cells (Rat1pEJ6.6) exhibited a pronounced left-shift of the pO_2 histogram with median values at 5 mmHg. About twice the number of tissue areas were at very low oxygenation levels with 35% of the values between 0 and 2.5 mmHg. The 10th and 90th percentile were at 1 and 37 mmHg. An even more marked shift in tissue oxygenation was observed in the v-myc immortalized and cHa-ras1-transformed Fischer rat tumour line (median pO_2 value = 1 mmHg). Here, almost 70% of the pO_2 values were detected between 0 and 2.5 mmHg. Both ras-transformed tumours grew much more rapidly than the spontaneously tumorigenic Rat1 line with volume doubling times ranging between 2.5 and 4 days.



(a) (b)

Figure 2. (a) Distribution of 2FDG at different times in a nu/nu mouse bearing a Rat1pEJ6.6 cell line tumour in a hind thigh. (b) High resolution imaging in the same tumour at 1 hour reveals a heterogeneous distribution of 2FDG; the two focal sites of increased 2FDG uptake in coronal section (B) and sagittal section (C). Coronal and sagittal section are reassembled from the measured data. (A) is a measured transverse section showing the tumour on the right, the bladder at the middle and the healthy thigh on the left.

Size-related changes in tissue oxygenation were studied in the Rat1pEJ6.6 tumours. Here, adequate oxygen levels were detected in small tumours with sizes between 50 and 100 mm^3 (median pO_2 value = 19 mmHg). Larger tumours with volumes up to 1000 mm^3 exhibited pO_2 histograms comparable to those described above, *i.e.* left-shifted distributions with median oxygen values at 4–5 mmHg. Thus increased tumour size correlated with a marked decrease in tissue oxygen levels.



(a)

(b)

Figure 3. (a) Distribution of 2FDG at different times in a nu/nu mouse bearing a Rat1 cell line tumour in a hind thigh. (b) High resolution images of the same tumour at 1 hour; transverse section (A) (showing the tumour on the right, the bladder at the middle and the healthy thigh on the left), coronal section (B) and sagittal section (C) through the centre of the tumour are presented.

Discussion

It is not necessary to correct data for recovery coefficient to obtain the value of glucose metabolic rate if the input function is determined using the blood pool data and the size of the regions of interest over blood pool and tissue are equal. Simulation of the effect of the recovery coefficient from the value of 0.1 to 0.7 on the glucose metabolic rate showed that, depending on the fitting and the statistical variation of data, the value of glucose metabolic rate will change by ±2%. If a recovery correction is used for blood pool activity or activity measured using blood samples, tissue data also must be corrected for recovery (Fig. 1).

The data obtained (Table I) clearly show that the glucose consumption is significantly increased in tumours compared to normal tissue and that it varies between different tumour lines being highest in Rat1pEJ6.6 tumours (13.4 ± 2.2 μmol/min/100 cm^3)

Table I. Regional glucose metabolic rate and median oxygen tension in tumours of different cell lines (including oncogene-transformed rat embryo fibroblasts). Tumours are size matched

	Normal tissue	Rat1 pEJ6.6	REFpneo MYCrasEpool	Rat1
Tumour volume doubling time (days)		2.5–4	2.5–4	28
Tumour volume (mm^3)[a]	—	363±70	411±45	421±51
Glucose metabolic rate (μmol/min/100 cm^3)[a]	4.3±0.8[b]	13.4±2.2	9.7±1.3	11.0±2.1
Number of studies	2	3	3	4
Tumour volume (mm^3)[a]		307±16	411±11	418±6
Median pO_2 (mmHg)	47[c]	5	1	12
Number of studies	10	10	10	10

[a] Mean ± SD.

[b] Skeletal muscle.

[c] Subcutis of the hind foot dorsum.

and lowest in REFpneoMYCrasEpool tumours (9.7 ± 1.3 μmol/min/100 cm^3). The glucose uptake in the Rat1pEJ6.6 line was marginally higher than the non-transformed Rat1 cell line and both were higher than the other transformed REFpneoMYCrasEpool line. The values obtained also show that glucose consumption increases with tumour growth (Table II). The high degree of resolution of PCR-I strikingly reveals the heterogeneous distribution of 2FDG in the large tumour (Fig. 2b (B) and (C); with two focal sites of increased 2FDG uptake) compared with the smaller tumour (Fig. 3b; single central site of increased 2FDG uptake).

Although the mechanism of increased accumulation of 2FDG in tumours is not fully understood, it most probably is related to the increased glucose utilization in tumours and the differences of glycolytic enzyme activity between tumour and normal tissues. It has also been recognized that the activity of key enzymes for glycolysis, including hexokinase, is increased in many tumours (Monakhov et al, 1978; Bustamante et al, 1981). More recent studies (Lowry et al, 1983; Nakashima et al, 1986; Nelson & Kabir, 1986) present evidence indicating that a form of hexokinase with a propensity for mitochondrial binding plays a key role in the high aerobic glycolysis that is typical of rapidly growing tumour cells. Hence this reaction may be primarily responsible for the intracellular trapping of 2FDG.

The critical aspect of using the Sokoloff model to determine glucose metabolic rate in tumours is the validity and value of the lumped constant. It may vary between healthy tissue and tumour and even between different types of tumours. In these calculations we have used the value 0.45 for all tissue types. Despite possible inaccuracies mentioned above, we believe that quantitative determination of glucose utilization is a valuable tool in assessing functional activities of different types of tumours. In addition, tumours based on oncogene-transformed cell lines provide useful experimental tumour models to study functional behaviour of tumours.

Owing to severe structural and functional abnormalities of the newly formed tumour vasculature (Peterson, 1979) a heterogeneously distributed and overall insufficient vascular network has generally been found in fast-growing malignant tumours (Vaupel et al, 1981). As a consequence, the supply of oxygen and nutrients is usually inadequate to satisfy the nutritional demands of the tumour tissue even at early growth stages (Vaupel,

Table II. Regional glucose metabolic rate and median oxygen tension in three different size groups of Rat1pEJ6.6 tumours

	Group 1	Group 2	Group 3
Tumour volume (mm^3)[a]	363±70	1277±69	3074±38
Glucose metabolic rate (μmol/min/100 cm^3)[a]	13.4±2.2	16.9±2.8	17.5±2.1
Number of studies	3	3	3
Tumour volume (mm^3)[a]	71±4	407±9	716±45
Median pO_2 (mmHg)	19	6	4
Number of studies	10	10	10

[a] Mean ± SD.

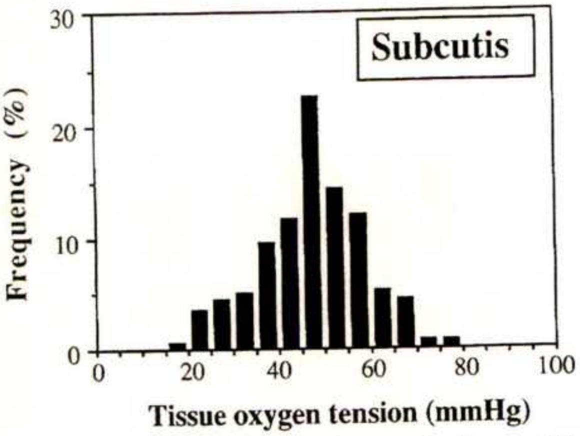


Figure 4. pO_2 histogram of mouse subcutis at the dorsum of the hind foot.

1977; Kallinowski et al, 1989; Vaupel et al, 1989b). In accordance with these findings, pO_2 levels lower than those in normal subcutis were measured in all tumours investigated here (Figs 4 and 5).

The spontaneously tumorigenic Rat1 cell line grew slowly allowing time for a more adequate vascular supply at comparatively low consumption rates. Since oxygen and nutrient levels within the tissue are determined by the relationship of supply and consumption, only 16% of the tumour mass was rendered hypoxic or even anoxic. Compared with a series of rapidly growing human tumours, studied as tissue-isolated xenograft preparations (Kallinowski et al, 1989), the Rat1 cell line, studied with high-resolution PET imaging, exhibited fairly low glucose consumption rates which also reflects the slow tumour growth. Considering a variety of human tumours, studied by PET techniques *in situ*, glucose uptake rates varied between 3 and 88 μmol/min/100 cm^3 (for a review see Vaupel et al, 1989b). Again, values measured in this study are at the low end of this range.

Accelerated growth rates were observed in both ras-transformed cell lines. Since rapid growth rates necessitate elevated consumption rates for oxygen and nutrients, severe tumour hypoxia was observed in tumours from both cell lines indicating an inadequate vascular supply. Recently, Ishikawa et al (1989) cotransfected ras-transformed NIH 3T3 cells with platelet-derived endothelial cell growth factor. They observed an increased vascularity *in vivo* but similar growth rates of secondarily transfected tumours as compared with the parent cell line. From these data, it may be concluded that ras transformation leads to severe tumour hypoxia by increasing the oxygen demand without adequately stimulating new vessel formation.

Perfusion differences of these tumours were assessed using a modified Sapirstein technique (Sapirstein, 1958). Here, radioactive indicator (thallium-211, Mallinckrodt, St Louis, Mo, USA) was injected into the vascular system and the animal was sacrificed after steady state conditions were reached. The fractional distribution at that time assesses relative changes of tissue perfusion unless the actual cardiac output can be measured. Using this technique on three to five animals each, the highest flow levels were obvious in Rat1 tumours (size range: 200–300 mm^3). Compared with these values, perfusion of Rat1pEJ6.6 tumours is reduced to 80% and that of REFpneoMYCrasEpool to 50%.

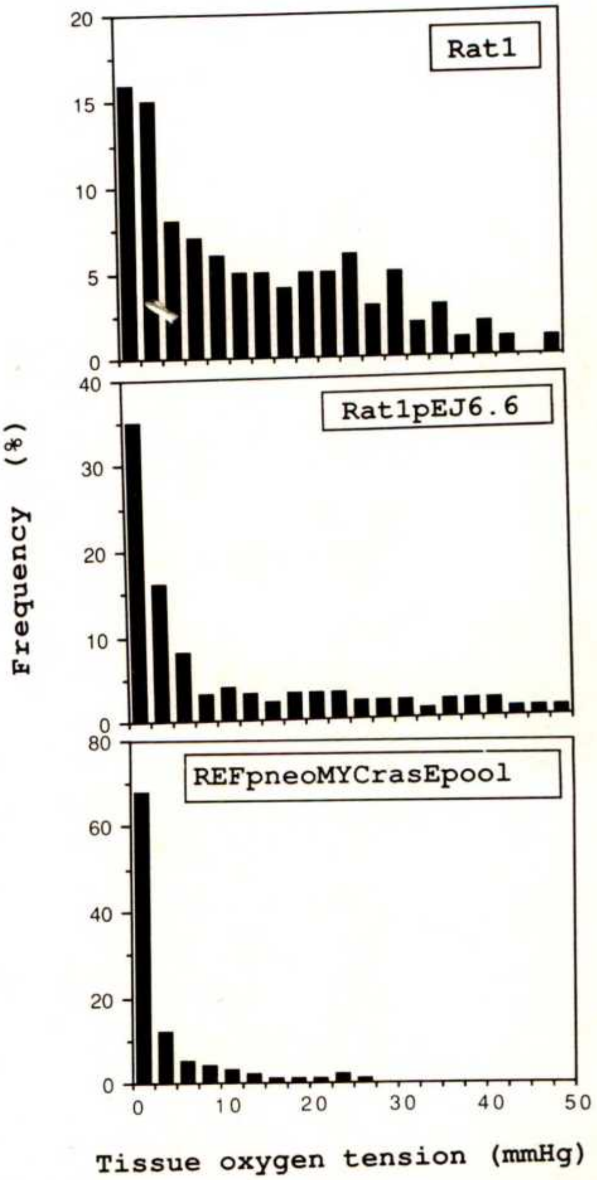


Figure 5. Frequency distributions of pO_2 values measured in Rat1, Rat1pEJ6.6 and REFpneoMYCrasEpool tumours with sizes around 400 mm^3.

Serial sectioning of two tumours of each cell line further substantiated these findings. Rat1 tumours exhibited large areas of vital tumour tissue with an adequate vascular supply (tumour size: 211 and 347 mm^3). In contrast, necrotic areas surrounded by a rim of vital tissue appeared in both Rat1pEJ6.6 and REF pneoMYCrasEpool tumours of comparable sizes.

However, considering both tumour lines independently, a more adequate tissue oxygenation and higher glucose metabolic rates were found in Rat1pEJ6.6 tumours as compared with REFpneoMYCrasEpool tumours which grew at similar rates. This may be explained by a more adequate vascular supply to Rat1pEJ6.6 tumours as compared with REF pneoMYCrasEpool tumours. An alternate explanation is that 2FDG uptake does not correlate directly with tumour growth or proliferation and merely reflects transport mechanisms and phosphorylating enzyme activity. This may vary from tumour to tumour independently of proliferation or malignant grade. Furthermore, this is unlikely to be a direct consequence of ras activation but may be related to other gene activation (Flier et al, 1987).

At later growth stages, the vascular supply is usually inadequate and inhomogeneously distributed over the tumour mass (Vaupel et al, 1981). In accordance with these findings, a reduction of tissue oxygen levels was observed in Rat1pEJ6.6 tumours exceeding 250 mm^3. This results in a reduction in oxidative glycolysis which might be partly compensated by an elevated glucose metabolic rate and an increased lactate production for tumour sizes up to 1500 mm^3. However, at even larger sizes (around 3000 mm^3), this mechanism becomes inefficient and no further increase in glucose metabolic rate is observed (Table II). On the other hand, this might also be explained by the above-mentioned and as yet unknown changes of glucose transporters and enzyme activity with tumour growth.

In this study, we have demonstrated the effectiveness of high resolution PET imaging combined with tissue oxygen measurements to gain further insight into mechanisms governing therapeutically relevant factors of the micromilieu of genetically defined tumours.

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Patient dose and risk in mammography

By J. Law, PhD

Department of Medical Physics and Medical Engineering, Edinburgh University and Western General Hospital, Edinburgh, UK

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Abstract. Patient dose in mammography is estimated by two different methods which are compared and which give good agreement. A mean tissue dose of about 1 mGy per film is found for a breast of 4.5 cm compressed thickness. Variables which affect dose are then considered quantitatively, including compressed breast thickness, tube potential, grids, magnification and beam collimation. The variables having the greatest effect are breast thickness and magnification. For example, an 8 cm breast receives about four times the mean tissue dose of a 3.5 cm breast. Similarly, using a magnification factor of about 2, dose is increased about four times in the primary beam, but the adverse consequences may be largely removed with conventional collimation to part of the breast only. Finally, the dose estimates are combined with existing data on breast cancer induction to predict the risk of carcinogenesis in a breast screening programme. For example, in a screening centre performing 15 000 examinations per year, only one induced cancer is predicted in about 7 years of screening under average UK conditions of age and breast thickness.

In mammography, as in other branches of radiology, there is a general conflict between image quality and patient dose. In establishing optimum technique, only good compression contributes both to improvement of image quality and patient dose reduction. At one time mammography was considered a high dose procedure. Since the general introduction of intensifying screens more than 10 years ago this is no longer the case, and doses are now usually well within the range of those reported by Shrimpton et al (1986) for eight common radiological examinations. Nevertheless it is still important that patient dose is regularly monitored and reviewed. Although image quality should be given priority, unnecessary dose must obviously be avoided.

The aims of this paper are to report briefly on current patient doses in the breast screening programme in Scotland, as derived by two different methods, and then to consider which variables affect patient dose and by how much. Compressed breast thickness is one such variable which has a considerable effect on patient dose but over which the radiographer and radiologist have little or no control. Other variables include tube potential (kV), use of grid, and beam collimation in magnification views, all of which are under user control but where improved image quality may require greater dose.

In conclusion, dose estimates are combined with risk factors to predict notional cancer induction rates in a breast screening programme.

Breast dose and dose distribution

At one time the surface or skin dose was often used in assessing breast dose and consequent risks. This was said to be because it represented the highest dose at any point in the breast, but it also had the attraction of being relatively easy to measure. However, attenuation of the beam as it passes through the breast is substantial, especially at around 28 kV as is commonly used now. Also it is believed that the main risk is one of cancer induction arising from dose to the glandular tissue, and therefore some attempt is usually made to allow for attenuation and to estimate the mean dose to glandular tissue. The physical distribution of glandular tissue within the breast is variable and not easily defined.

In this paper, skin dose will be estimated by two different methods. Both estimates will be converted to mean breast dose by using data from IPSM (1989). This is claimed to give mean glandular dose for a 4.5 cm compressed breast, and allows for attenuation through a breast of that size. Mean breast dose for breasts of other thicknesses is estimated from that for the 4.5 cm breast by extrapolation of the attenuation curve which is assumed to be smooth. This is equivalent to assuming that the glandular tissue is uniformly distributed through the whole breast.

Measurement of surface dose for a 4.5 cm compressed breast

The first method to be described is that given by IPSM (1989). The attenuation properities of 4 cm of Perspex (poly(methyl methacrylate)) are considered to be equivalent to those of a 4.5 cm compressed breast. Perspex blocks to a thickness of 4 cm are placed on the grid cover with a loaded cassette beneath, and an exposure made under AEC at 28 kV or the tube potential in clinical use if different. The mAs delivered is noted for a series of exposures, and an ion chamber is then used to measure the tube output at the same tube potential and corresponding mAs values. The compression plate is used in its normal position in both cases. The ion chamber is also used to measure the half-value thickness (HVT) of the beam in aluminium of adequate purity. Two factors are then obtained from tabulated values for the measured HVT. The first converts the air kerma for the Perspex phantom to that for a standard 4.5 cm

Table I. Measurements of surface dose to a 4.5 cm compressed breast on various X-ray sets during 1989

		Surface dose estimation, mGy for 4.5 cm compressed breast		
Date	X-ray set	Predicted (IPSM, 1989)	Measured	Ratio
January	A	3.3	4.4	1.3
	B	2.9	4.0	1.4
	C	6.8	4.8	0.7
	D	3.0	3.3	1.1
June	A	3.5	4.3	1.2
	B	3.1	4.7	1.5
	C	3.9	3.0	0.8
	D	4.2	3.9	0.9
	E	3.6	2.8	0.8
December	A	3.2	4.6	1.5
	B	3.9	5.2	1.3
	C	2.3	3.7	1.6
	D	4.2	3.8	0.9
	E	3.7	3.5	1.0

Mean ratio measured/predicted: 1.14±0.08.

breast, and the second converts the latter to mean glandular tissue dose.

The second method is based on data obtained from a large number of breasts undergoing X-ray examination. Originally, TLD discs were placed on the skin on a corner of the breast during each X-ray exposure, but the results were considered to be no more accurate than from the following method which is simpler and quicker. For a series of (say) 50 patients, taken consecutively or otherwise randomly selected, the compressed breast thickness and also the mAs delivered is noted by the radiographer for each film taken. The thickness may be measured directly by a tape measure, or using the X-ray set indication from the compression plate height, or by measuring from tube housing to compression plate and subtracting. All three may present problems and a combination may be required. A graph is plotted of mAs against thickness, and a smooth curve drawn through the points which are usually well scattered. The mean mAs for a breast of 4.5 cm (or any other thickness) can be read off, and the air kerma for the breast for that mAs can then be estimated as before using an ion chamber. The mean glandular tissue dose is then calculated using the second of the two factors from IPSM (1989) referred to above.

The advantages of the first method are that it is much quicker and can be used before the X-ray set goes into routine use. The second method is more directly related to breast doses actually received. The scatter in the plotted data arises mainly from the normal variability of breast structure and density in the population, and this information is of interest in itself. Both methods are probably uncertain to ±20% or more. Until more experience in the field has been reported, it seems worthwhile to use both methods regularly.

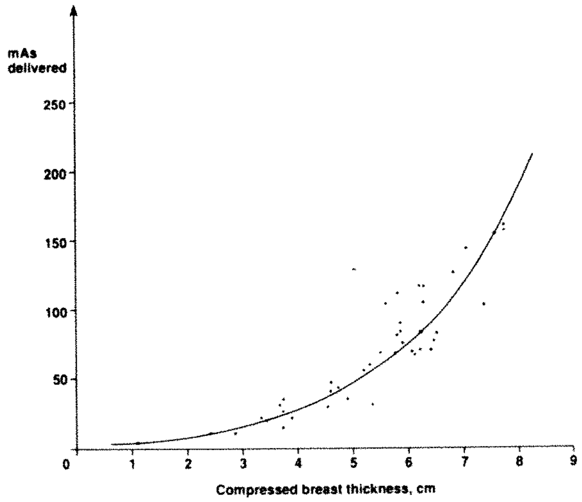

Figure 1. Relative exposure in relation to compressed breast thickness.

Measurements of breast surface dose

Results of measurements by both techniques on 14 occasions covering five X-ray sets are presented in Table I. Three of the sets are Siemens Mammomat 2's; the other two are a CGR 600T and Philips Diagnost U. All these sets are used in the breast screening programme in Scotland. An example of the data obtained for one X-ray set by the second ("thickness") method is shown in Fig. 1. For any given X-ray set the results vary from one occasion to another by up to about 40%, but these apparent changes may be largely due to random uncertainties.

The mean ratio of dose estimation from the second method to that from the first is 1.14±0.08. It is slightly higher for sets A and B which are a Siemens Mammomat 2S and a 2 respectively, but slightly lower for set E which is also a Siemens Mammomat 2S. Set C, which is a Philips set, shows more variation through the year but its mean result is close to the others. Set D is a CGR 600T and is more self-consistent. The degree of agreement between the two techniques is reasonably good, and closer agreement should not be expected.

Table II outlines the calculation of mean breast dose from surface doses. The HVT on each of the X-ray sets was measured in the same months as the dose estimates were obtained but did not vary significantly for any X-ray set, and averages for the year have been used for these and for the surface doses. The "thickness" method has been used for surface dose measurements as this is based on results from breasts examined in a screening programme rather than on results obtained with Perspex blocks.

Effect on dose of variations of breast thickness

The major consequence for breast dose of a change in breast thickness is that the mAs required under AEC is increased considerably as the thickness increases, as can be seen in Fig. 1. Relative values of mAs for various

Table II. Estimates of mean dose to breast tissues calculated from measured surface doses (averages for 1989, thickness method) for a 4.5 cm compressed breast

X-ray set	Mean HVT at 28 kV (mm Al)	Conversion factor from IPSM (1989)	Mean breast dose (mGy)
A	0.34	0.203	0.9
B	0.35	0.208	1.0
C	0.37	0.218	0.8
D	0.36	0.213	0.8
E	0.34	0.203	0.6

Mean for five X-ray sets: 0.8 mGy.

Table III. Relative mean dose to breast tissue for different compressed breast thicknesses, normalized to 4.5 cm (28 kV, with grid)

Compressed breast thickness (cm)	Relative surface dose	Factor to mean breast dose[a]	Relative mean dose to whole breast
3.5	0.64±0.03	0.263	0.81
4.5	1.0	0.208	1.0
5.0	1.23±0.02	0.188	1.1
6.5	2.5 ±0.1	0.145	1.7
8.0	5.6 ±0.5	0.118	3.2

[a] Based on factor in IPSM (1989) for 4.5 cm compressed breast and HVT=0.35 mm Al.

thicknesses have been obtained from 10 graphs similar to Fig. 1, all obtained from the five X-ray sets referred to in Tables I and II. These relative values, with their standard errors (68% confidence limits), are given in Table III.

Mammography X-ray sets usually work with a constant focus–film distance (FFD), typically 60 cm, and that FFD applies to contact films on all five X-ray sets referred to here. For a given mAs value, surface doses will vary with breast thickness and hence focus–skin distance (FSD) approximately according to inverse square law. Thus, in comparison with a 4.5 cm compressed breast, surface dose per mAs will be approximately 4% lower for a 3.5 cm breast and 13% higher for an 8 cm breast. This effect has been allowed for in the relative skin doses of Table III.

The conversion factors to mean breast dose given by IPSM (1989) and used in Table II are closely related to percentage depth doses. They are only quoted in that publication for a thickness of 4.5 cm, but at all HVT values used here the beam intensity at or beyond this thickness is only a few per cent. By treating these factors as mean percentage depth doses it is possible to derive corresponding factors for other breast thicknesses, without introducing further errors of more than about 5%, *i.e.* well within experimental errors already present. A further small correction should in principle be made to allow for changes in percentage depth dose arising from change in FSD. However, this is less than about 1% for contact films because the great majority of the dose is deposited in the first 2 cm below the surface.

Relative mean doses to the whole breast, calculated in this way from the skin doses for various thicknesses, are given in the last column of Table III.

Effect on dose of variations in tube potential

If the tube potential is increased, the mAs recorded under AEC decreases. The tube output (mGy/mAs) increases with tube potential, but the net effect is usually a decrease in surface dose. In ordinary screening practice the tube potential is seldom varied, so that direct evidence from clinical practice on dose effects is not readily obtainable. Some evidence is available from AEC test films of Perspex blocks, however, and relative mAs values for 25, 28 and 30 kV are presented in Table IV, averaged for the five X-ray sets referred to in previous tables, together with the corresponding surface doses allowing for change in tube output with tube potential. Experimental evidence from other work suggests that the HVT changes by approximately 0.01 mm Al for a change of 1 kV between 25 and 30 kV. This, together with the conversion factors from IPSM (1989), has been used to estimate relative mean breast doses for 4 cm Perspex blocks or 4.5 cm compressed breast thickness as shown in Table IV.

For other block thicknesses, also at 25 to 30 kV, relative mean breast doses have been calculated in the same manner, using data from two X-ray sets only. Factors to convert from surface dose to mean breast dose were estimated as for Table III, and a correction of 8% was made to allow for the FSD change of 2 cm for blocks of 2 cm or 6 cm thickness. The results are given in Table V. The two X-ray sets from which these data were taken were Siemens Mammomat 2's, chosen because they lay closest to the means of five sets used in Table IV. This explains the apparent inconsistency between Tables IV and V for 4 cm block thickness.

Effect of use of a grid

The grid factor at 28 kV has been estimated for three different manufacturers' products in the following way.

Table IV. Relative mAs and dose values for different tube kV, for 4 cm Perspex phantom under AEC

	Tube kV		
	25	28	30
Relative mAs values	2.8±0.4	1.0	0.70±0.02
Relative tube output (mGy/mAs)	0.68	1.0	1.30
Relative skin dose	1.9	1.0	0.91
Mean HVT (mm Al)	0.32	0.35	0.37
Factor to mean breast dose (IPSM, 1989)	0.193	0.208	0.218
Relative mean breast dose	1.8	1.0	0.95

Table V. Relative mean dose values for different tube kV and phantom thickness under AEC

Perspex phantom thickness (cm)	Tube kV 25	28	30
2	0.47	0.36	0.36
4	1.5	1.0	0.95
6	3.9	2.8	2.3

A film was exposed in a cassette beneath the grid in the normal manner using AEC, with a 4 cm Perspex block above the grid. The mAs delivered was noted and the film was processed. Its density was measured and was in the range 1.0–1.4 in all cases. The same cassette was then used above the grid but below the same 4 cm Perspex block, and exposed under manual control with an mAs value just under half that recorded with the first film. The film density was similar to that of the first film, and the small difference was corrected for by simple proportion. The vertical displacement of the cassette was about 3 cm, and the effect of this was corrected for by inverse square law. The grid factor was calculated from the ratio of the mAs values with these two corrections.

The results of two estimates on each of the three X-ray sets was 2.30±0.04. There was no significant difference between the Philips, CGR and Siemens grids in this respect.

Effect of magnification

Magnification techniques are liable to increase breast dose very substantially for a number of reasons. The breast is much closer to the focus while the FFD is either unchanged or increased, requiring greater mAs for a given film density. Film density may also be reduced because of the reduction in scatter reaching it, and this may require a further increase in mAs, but the absence of a grid in magnification makes this difficult to predict quantitatively. A small reduction in mean breast dose for a given surface dose will apply because the FSD is much reduced. Beam collimation, however, is sometimes used in magnification and will reduce the quantity of tissue irradiated and any consequent risk.

The IPSM (1989) makes no specific comment on doses with magnification, so that their predictive method of dose estimation is less easy to apply. Comparing mAs values for 4 cm Perspex blocks under contact and magnification conditions is not valid if the film densities differ substantially, as is sometimes the case. Instead, the "thickness" method has been applied as for contact films, and the mAs required for a 4.5 cm compressed breast has been used with direct measurements of tube output above the magnification platform to derive estimates of surface dose within the primary X-ray beam.

On one CGR 600T X-ray set, four different sets of data for magnification films have been used to derive a mean ratio for magnification to contact film surface dose of 5.4±0.4, using results both for 5 cm and 4.5 cm compressed thickness. On this X-ray set, magnification films are taken at 26 kV and contact films at 28 kV. On one Siemens Mammomat 2, where 28 kV is used for both contact and magnification films, one set of magnification data from 40 patients gave a dose ratio of 3.5. The difference between these two values is largely explained by the difference in practice over tube potential between the two centres. The magnification factor was nominally 2.0 on both sets.

It may be assumed that the IPSM conversion factors from surface dose to mean breast dose are unchanged with magnification, except that the much shorter FSD under magnification leads to a small relative reduction in percentage depth dose. Since most of the dose is deposited in the first 2 cm, the surface dose ratio should be reduced by about 6% in estimating the mean breast dose ratio. There is urgent need for more data on patient dose with magnification, but at present a dose ratio of between 3.3 and 5.0, depending on kV policy, seems the best estimate for a magnification factor of 2.

In the foregoing discussion it was assumed that there is no beam collimation within the volume of the breast. Such collimation is not normally employed in contact films because the whole of the breast needs to be included. With magnification, however, where the region of interest may be small and already defined from a previous contact film, beam collimation may be possible, at least with some patients. Practice seems to vary between different UK centres on this matter, and the risk of missing important features in a collimated film must be recognized. Nevertheless, beam collimation will significantly reduce the quantity of breast tissue irradiated and hence the resulting risk of carcinogenesis. In some cases, where only about one fifth of the breast falls within the beam, the risk may be comparable with that from a contact film. (This assumes that the absence of the grid balances the increase in mAs needed to compensate for a reduced amount of scatter reaching the film, as mentioned above.)

Discussion

The general practice of using grids, in spite of the increased dose, results from a concern for image quality and is unlikely to be reversed. For similar reasons, tube potential remains relatively low; 28 kV is currently a well established figure. Breast thickness under compression is at least as important as these in its bearing on breast dose. The variations reported here underline the importance of continuing to apply firm compression, not only for its value in improving image quality but also for the dose reduction it brings with it. It is the one parameter under the control of radiologist and radiographer which tends both to improve the image and to reduce the dose. This point should be kept in mind if its regular use were ever reconsidered.

Magnification causes a substantial increase in patient dose though the consequences may be mitigated if the beam is reduced in size. The greater the degree of magnification the greater the increase in dose. A clear

Table VI. Cancer induction rates, per million examinations at 1 film/breast, at a mean breast dose of 1 mGy/film, against age and breast thickness

Age (years)	Compressed breast thickness (cm)				
	3.5	4.5	5.0	6.5	8.0
45	10.7	13.2	14.5	22.4	42.2
50	8.3	10.2	11.2	17.3	32.2
55	6.3	7.8	8.6	13.3	25.0
60	4.4	5.4	5.9	9.2	17.3
65	2.9	3.6	4.0	6.1	11.5

Table VII. Average years of screening per cancer induced, assuming 15 000 examinations per year, with allowance for magnification films (see text), against age and breast thickness

Age (years)	Compressed breast thickness (cm)				
	3.5	4.5	5.0	6.5	8.0
45	4.9	4.0	3.7	2.4	1.3
50	6.4	5.2	4.8	3.1	1.7
55	8.5	6.9	6.2	4.0	2.2
60	12.1	9.8	9.0	5.7	3.1
65	18.4	14.4	13.4	8.7	4.6

advantage in clinical films is sometimes claimed for magnification factors of around 1.5, but other radiologists find that a magnification of close to 2 is more valuable. Magnification much greater than 2 is probably not feasible without substantial redesign of tube housing, or an increased FFD, which in turn requires an increased dose. Quite apart from that, with greater magnification the limit on resolution is set by focal spot size and degree of magnification rather than film–screen characteristics.

The effect of magnification on patient dose within the primary X-ray beam is reasonably clear, but beam collimation can substantially reduce the consequent risk to the patient. Since magnification can lead to a large increase in patient dose, and a relatively high dose in thick breasts, collimation should always be used where it is unlikely to cause the film to be repeated.

The choice of film–screen combination obviously influences dose, and currently available films vary up to a factor of 4 (Law & Kirkpatrick, 1990), though screen speeds are much less variable. Again, faster films usually give poorer images, and a film speed around that of Fuji NH or MA, or Dupont Microvision, seems reasonable. It is interesting to find that radiologists' reluctance to use slower film is sometimes influenced not by the increased dose but by the desire for shorter exposures and less risk of motion unsharpness.

Cancer induction in relation to dose

This was the subject of an earlier paper (Law, 1987) which compared cancer detection rates in a screening programme with future cancers which might be induced by the X-ray dose. A mean breast dose per film of 1 mGy was used then, and is used again here as a "round number" value rather than the 0.8 mGy per film given in Table II. A cancer induction rate of 6 cases per 10^4 women examined per Gy per year, from 10 years post-exposure for the rest of life, was taken as a cautious estimate, *i.e.* slightly high rather than slightly low. This was not influenced by atom bomb survivor data, which at that time looked lower than other data for breast cancer. Consequently the current revisions to the atom bomb data do not require a change to this figure (Shimuzu et al, 1987).

A second consideration here is the photon energy in mammography and the question of relative biological effectiveness. An increased RBE of around 1.3 relative to higher photon energies has been suggested (Brenner & Amols, 1989), which if applied here would require a cancer induction rate of 8 per 10^4 per Gy per year. For the present, the former value of 6 will be retained; in the tables which follow, readers may apply a correction factor of 1.3 if they wish, or if future evidence requires it.

Law (1987) concluded that cancers detected exceeded those which might be induced by a margin which varied with age of the woman, and between first and repeat examinations, but was always within the range 200–1000 : 1 even with cautious assumptions regarding induction. Further consideration of the implications of this may be found in Law (1988).

In Table VI, a mean breast dose of 1 mGy per film is taken for a 4.5 cm breast, and a screening programme involving one film per examination per breast is assumed. Cancer induction rates at ages 45–65 years are taken from Law (1987) and used to produce rates per million examinations for different breast thicknesses, using relative doses from Table III. The results show a substantial variation from well over 30 for the younger woman with a thick breast to less than 3 for an older woman with a thin breast. In this context it is unfortunate that younger women tend to have denser breasts but not necessarily thicker ones under compression.

Lest these cancer rates appear to be high, it may be instructive or more useful to present this data in a different form. In a given screening centre, 15 000 examinations per year would be a reasonable estimate for a single X-ray set. The data in Table VI can then be used to estimate the *average* time required, on a statistical basis, to produce a single future cancer, at a range of ages and for various breast thicknesses. In practice, up to about 10% will be recalled for a repeat contact film and about half these will have a magnification film, mostly on one breast only. These additions to the dose burden will reduce the calculated times by about 1.25, and this has been allowed for in arriving at the figures shown in Table VII. That assumes no beam collimation with magnification; if only half the breast is included in the beam in such views then the corresponding factor will be about 1.12 and the figures in Table VII could be lengthened by about 10%.

The IPSM (1989) suggests 4.5 cm as a reasonable average thickness for breasts under compression. The data obtained in the course of this work, of which Fig. 1 is a typical example, suggest that a figure in the region of 5.5 cm is more reasonable for a screening population, at least in Scotland. This is relevant when considering Tables VI and VII.

Conclusion

On the basis of the figures in Table VII, and allowing for the spread in breast sizes, an overall mean time to produce one future cancer per X-ray set in the current UK screening programme might be around 6–9 years. Here it may be important to recall that cancer induction estimates are all based on the well known extrapolation from high to low radiation doses. It has been suggested by Roebuck (1986) that there is as yet no firm evidence that any additional breast cancers are induced in the age group of the screening programme and at the doses concerned, which are low. Even for those with thick breasts, and for whom the dose is well above average, there appears to be no reason to alter the view that image quality should take precedence over dose reduction, especially since good image production is more difficult as breast thickness increases.

Acknowledgments

I should like to thank all radiographers in the Scottish Breast Screening Programme for their co-operation in obtaining patient data for this work.

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Case reports

Calcified splenic and portal vein thrombosis: an unusual cause of multiple high amplitude echoes in the spleen

By Hugh Logan, FFR, RCSI and *Hylton Meire, FRCR

Kings College Hospital, Denmark Hill, London SE5 9RS

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Keywords: Ultrasound, Splenic vein thrombosis, Portal vein thrombosis, Calcification

Calcification in the walls of the portal vein and in portal and splenic vein thrombosis is well described (Mobeg, 1943; Magovern & Mensham, 1954; Sherrick et al, 1964; Adler, 1979; Mata et al, 1987). Multiple calcific foci in the splenic parenchyma is an unusual but well recognized appearance that is usually attributed to calcified granulomata due to previous tuberculosis or parasitic infestation (Meire, 1988). We report a case of multiple calcific foci in an enlarged spleen that were unequivocally localized to the lumina of tributaries of the splenic vein on ultrasound in a cirrhotic patient with cavernous transformation of the portal vein and documented portal vein thrombosis.

Case report

A 57-year-old English railway worker has been under the care of the Liver Unit in King's College Hospital for the past 20 years for cryptogenic hepatic cirrhosis with protal hypertension. He has had several episodes of haematemesis from gastric and oesophageal varices, managed with injection sclerotherapy. In 1981 an attempt was made to embolize bleeding gastric

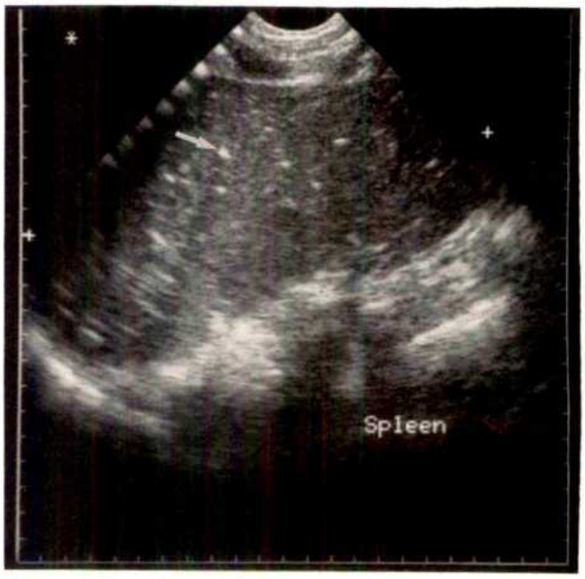
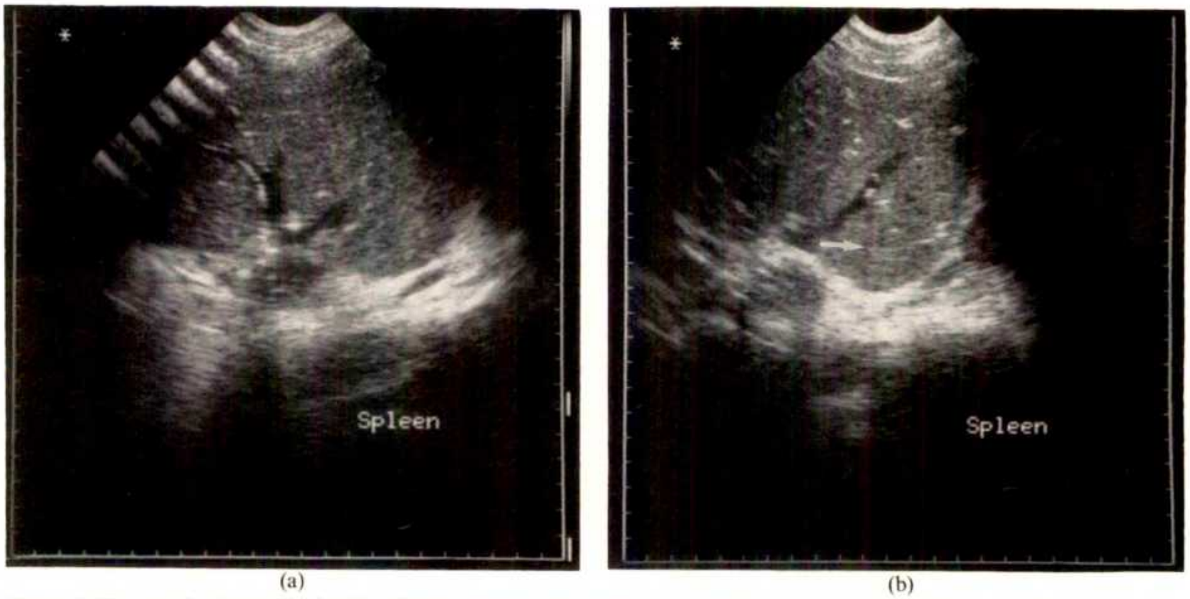


Figure 1. The spleen. It is markedly enlarged, and there are multiple foci of calcification with acoustic shadowing (arrow).



(a) (b)

Figure 2. The splenic hilum. The highly reflective material lies within the vessel lumen. Acoustic shadowing is shown (arrow).

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* Author for correspondence.

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varices, and at angiography the right main branch of the portal vein was found to be occluded. In 1986 at ERCP portal vein calcification was noted.

The portal vein was found to be dilated on ultrasound in 1981, and by 1987 there was cavernous transformation, with no main portal vein identifiable. Multiple high level echoes were seen in the spleen in 1986 for the first time.

At the most recent examination the liver was found to be small and there was cavernous transformation of the portal vein. The spleen was very large and contained multiple strong echoes, some of which showed acoustic shadowing (Fig. 1). From the splenic hilum to the centre of the spleen all of these echoes were demonstrated to lie within the lumina of tributaries of the splenic vein (Fig. 2).

Discussion

Dense calcification in the main portal vein is readily apparent on plain radiographs, but its strong echoes on ultrasound may be wrongly attributed to bowel gas. In this case the relationship of the calcific foci in the spleen to the veins was not apparent until intrasplenic veins were scanned longitudinally. It is probable that other cases of calcific foci in the spleen that are attributed to old granulomata, in an appropirate clinical setting, are in fact due to calcified thrombus.

Since identification of the nature and location of the splenic calcification in this patient identical intravascular calcifications have been identified in a further three patients with long standing splenomegally complicating portal hypertension.

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Papillary cystic tumour of the pancreas: findings at computed tomography and ultrasound

By G. W. L. Phillips, MA, MRCP, FRCR, *S. T. Chou, MB, FRCPath, FRCPA and J. Mulhauser, MB, BS

Departments of Radiology and *Pathology, Repatriation General Hospital, Heidelberg, Victoria 3081, Australia

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Keywords: Papillary cystic tumour, Pancreas

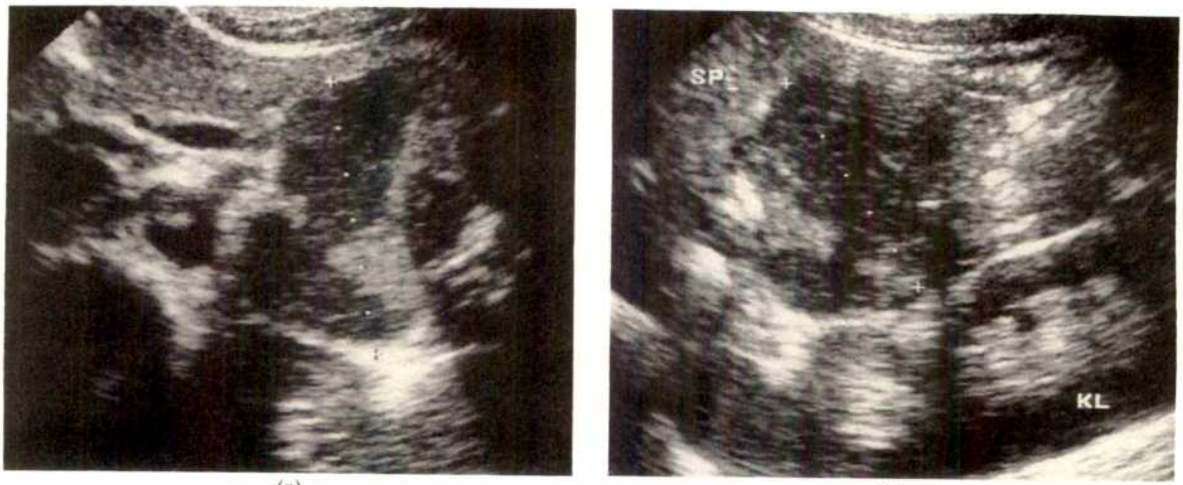
Papillary cystic tumour is a rare pancreatic neoplasm which occurs typically in young females and is of importance because of its good prognosis. We describe the computed tomography (CT) and ultrasound features correlated with pathological findings in a case where the tumour was discovered as an incidental finding.

Case report

A previously well 17-year-old female presented with right upper quadrant pain. A clinical diagnosis of cholecystitis was made and an ultrasound examination requested. This confirmed the presence of multiple gallstones and also demonstrated a 6 cm diameter complex cystic mass with solid elements in the region of the tail of the pancreas (Fig. 1). Computed tomography demonstrated a similar appearance with solid elements and cystic areas of CT numbers +20 to +40 HU consistent with haemorrhage or necrosis but in addition revealed a small solitary focus of calcification at the periphery of the mass (Fig. 2).

At laparotomy the mass was seen to protrude from the tail of the pancreas and could be readily enucleated. The gallbladder, which contained multiple mixed stones and showed chronic non-specific inflammation, was also removed. Subsequent histology of the pancreatic mass demonstrated an encapsulated neoplasm comprising sheets and papillary fronds of uniform small polygonal cells interspersed with old and recent haemorrhage and scattered cholesterol crystals (Fig. 3). Tumour invasion of the capsule was evident in foci but no extracapsular deposits were seen. The histological features were characteristic of papillary cystic tumour of the pancreas.

Address for correspondence: Dr G. W. L. Phillips, Department of Radiology, Repatriation General Hospital, Heidelberg, Victoria 3081, Australia.



(a) (b)

Figure 1. (a) Transverse ultrasound scan demonstrating a 6 cm mass lateral and posterior to the left lobe of the liver. The mass contains some solid tissue but is predominantly hypoechoic, consistent with areas of haemorrhage or necrosis. (b) Longitudinal ultrasound scan demonstrating the mass lying between the spleen (SP) and left kidney (KL).

Discussion

Papillary cystic tumours of the pancreas are rare. Approximately 90 cases have been reported and the ultrasound and CT findings documented in approximately 10 cases. Ninety-five per cent of these tumours occur in females and 85% present by the age of 30 (Cubilla & Fitzgerald, 1984; Friedman et al, 1985). Tumour tissue has been demonstrated to contain receptors for oestrogen and progesterone (Ladanyi et al, 1987) and this may explain the age and sex distribution.

Most patients present with signs and symptoms of an abdominal mass but others have been detected incidentally as in our case. The mean size is 12 cm, considerably larger than in our case, and this finding is in keeping with the observation that most of these present relatively late due to symptoms because of the large size of the tumour. Those found incidentally, as in our case, present earlier and are therefore smaller.

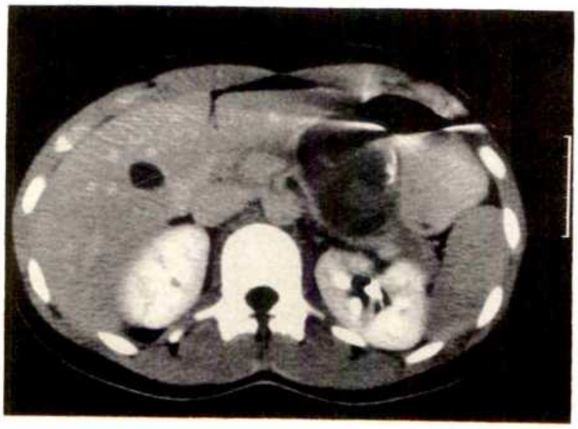


Figure 2. Axial CT scan again demonstrating the part solid, part cystic nature of the mass. These scans also demonstrate peripheral calcification, and the relation of the mass to the tail of the pancreas can be appreciated.

These tumours are most commonly located in the pancreatic tail (Cubilla & Fitzgerald, 1984). They have a varied appearance on CT and ultrasound. All reported cases appear well circumscribed (Friedman et al, 1985; Kim et al, 1985; Farman et al, 1987) but are of variable internal architecture. They are most commonly of mixed cystic and solid components but may be almost entirely solid or else cystic with thick walls. The cystic areas represent haemorrhage and/or necrosis. Calcification is an infrequent finding and when described occurs in the periphery of the capsule as in our case.

Pathologically the tumour in our case had both macroscopic and microscopic features of papillary cystic tumour similar to those described previously (Cubilla & Fitzgerald, 1984; Friedman et al, 1985; Kim et al, 1985).

Prognosis after complete resection is good. Although most of the tumours appear benign, the presence of focal capsular invasion as in our case indicates malignant potential of the tumour. Local recurrence has been documented many years after surgical removal and a few cases of metastases have been described (Kaufman et al, 1985; Rustin et al, 1986). These tumours are consequently regarded as being of low grade malignant potential best treated by surgical removal and long term follow-up.

The differential diagnosis is of ductal cell adenocarcinoma, microcystic adenoma, mucinous cystic neoplasms (cystadenoma and cystadenocarcinoma) and islet cell tumours. Although the final diagnosis can only be established by pathological assessment, the diagnosis and its attendant good prognosis should be considered likely when a well circumscribed partly cystic, partly solid

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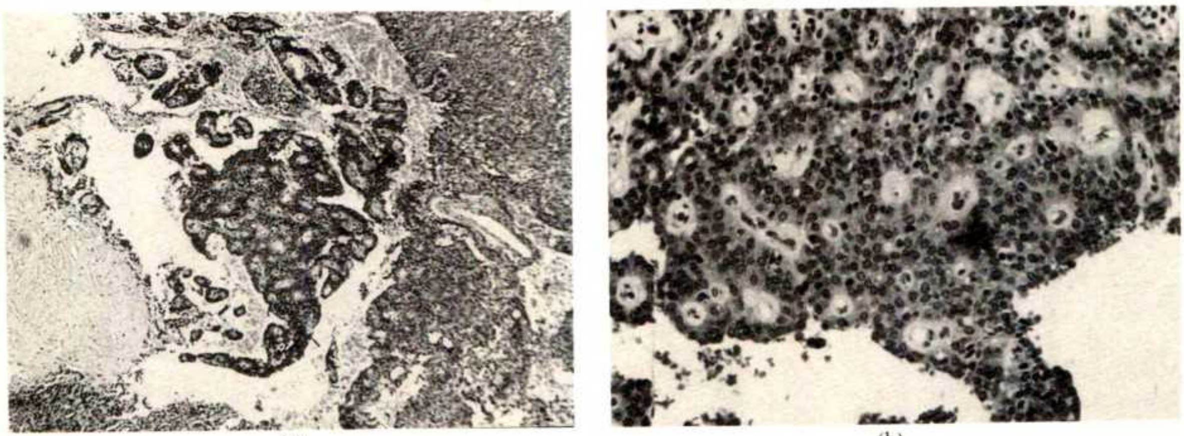

(a) (b)

Figure 3. (a) Microphotograph of the cystic tumour showing fibrous wall (left) and papillary fronds and sheets of tumour cells projecting into the cavity (H. and E., original magnification × 40). (b) Higher magnification of Fig. 3(a) showing papillary fronds with fibro vascular cores covered by uniform small polygonal cells (H. and E., original magnification × 100).

mass is seen in the tail of the pancreas in a young female patient.

Acknowledgments

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Late presentation of bone metastases in phaeochromocytoma

By I. Zammit-Maempel, MRCP, FRCR, R. J. Johnson, MRCP, FRCR and *H. Rao Gattamaneni, MD, FRCR

Departments of Diagnostic Radiology and *Radiotherapy, Christie Hospital and Holt Radium Institute, Wilmslow Road, Withington, Manchester M20 9BX, UK

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Keywords: Bone metastases, Phaeochromocytoma

Phaeochromocytoma is a relatively rare tumour of neuroectodermal origin that is said to occur in up to 0.1% of patients with diastolic hypertension (Magner & Gifford, 1977). Around 10% of phaeochromocytomas are malignant and bone is the most common site of metastases. We present two cases of malignant phaeochromocytoma presenting 4 years and 14 years after diagnosis with bone metastases.

Case reports

Case 1

A 16-year-old girl presented in 1967 with anxiety, headaches, sweating, palpitations and an elevated blood pressure at 180/130. Twenty-four-hour urine collection confirmed the diagnosis of a phaeochromocytoma with elevated urinary metadrenalines. At laparotomy a right adrenal tumour, histologically confirmed as a phaeochromocytoma was removed together with the right kidney, to which it was adherent.

The patient re-presented in 1981 with a 1-year history of right hip pain. Plain radiographs showed a lytic area in the neck of the right femur (Fig. 1) which was shown to be a solitary hot spot on isotope bone scanning. The right hip was explored and a bone graft inserted. Histology was initially reported as showing lymphoma but on review a diagnosis of metastatic phaeochromocytoma was made. Twenty-four-hour urinary free catecholamines were significantly raised. The patient was treated with a single radiotherapy exposure to the right femur.

The patient remained well until 1987 when she complained of increasing bouts of sweating and tremor, weight loss and a 4-day history of swelling in her left parieto-occipital region. She was hypertensive with elevated urinary metadrenaline and plasma noradrenaline but normal thyroid function tests. Chest radiography revealed intrapulmonary metastases while skull radiography showed a destructive lesion in the left posterior parietal region (Fig. 2). Meta-iodobenzyl guanidine (MIBG) scan confirmed markedly increased uptake in the left posterior parietal region but also showed some increased activity at C1, the right iliac crest and right proximal femur.

Her blood pressure was controlled with labetolol and the metastatic deposits treated with a course of iodine 131 MIBG with initial regression. A year later, however, the left parietal and chest metastases increased in size. A computed tomography brain scan showed a large lytic lesion in the left parietal bone with associated enhancing soft tissue component extending both intra- and extra-cranially (Fig. 3). The chest and skull vault metastases were treated with megavoltage external radiotherapy. In August 1989 she complained of increasing irritability and chest radiography revealed further increase in size of the multiple pulmonary metastases. In May 1990 she developed papilloedema and multiple cranial nerve palsies suggestive of brain metastases which were, however, not confirmed on computed tomography scan. She improved with further radiotherapy but died in June 1990, presumably from her disease.

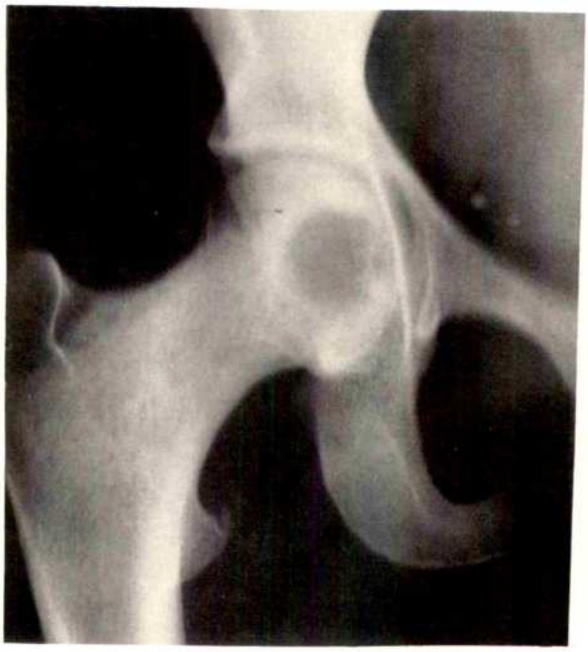

Figure 1. Right hip tomogram showing well defined lytic deposit.

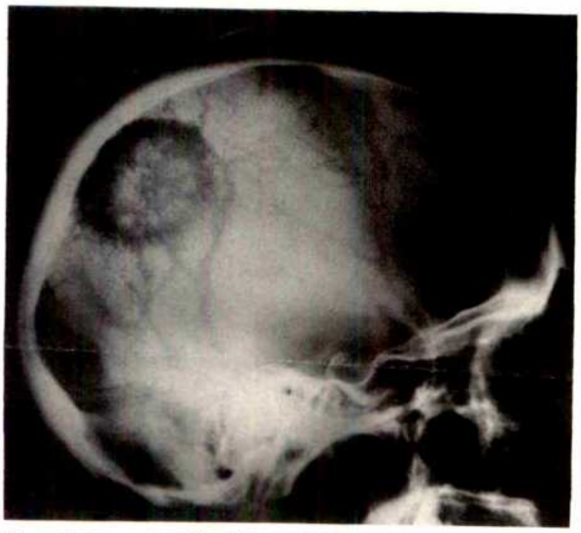

Figure 2. Lateral skull radiograph showing lytic parietal lesion with enlarged vascular grooves.

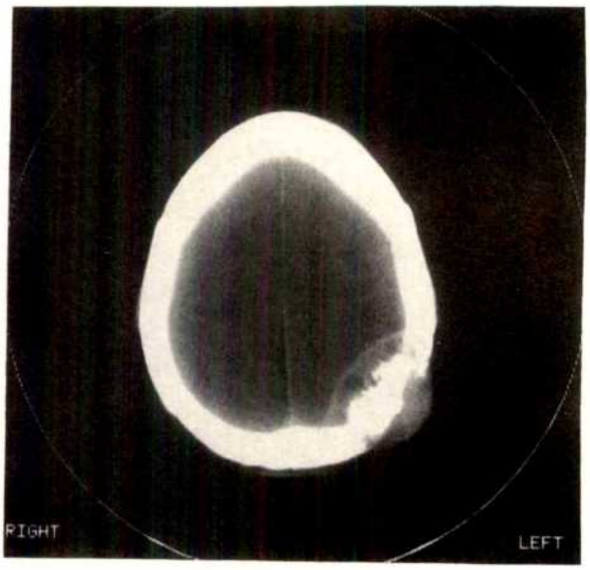

Figure 3. Post contrast brain computed tomograph showing destructive lesion in left parietal region with enhancing soft tissue extending both intra- and extra-cranially.

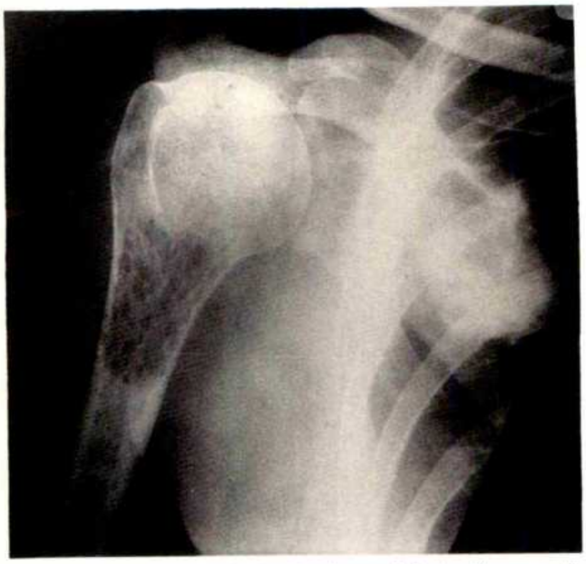

Figure 4. Lytic deposit within right humeral shaft. Also note rib metastasis with associated pleural based mass.

Case 2

A 9-year-old girl presented in 1973 with poor eyesight and a 1-year history of intermittent malaise, backache, constipation, palpitations and sweating. On examination she had a grade IV hypertensive retinopathy, with an elevated blood pressure at 205/150. A diagnosis of phaeochromocytoma was confirmed by elevated urinary catecholamines. At operation a locally invasive tumour, histologically confirmed to be phaeochromocytoma, was incompletely excised. A limited skeletal survey, including skull and chest radiography at this stage revealed no evidence of metastases. The patient remained well for a year when hypertension recurred accompanied by elevated urinary catecholamine excretion. At surgery, incomplete excision of recurrent tumour extensively invading surrounding structures was again carried out. In 1976 catecholamines were again noted to be raised but at laparotomy, a large inoperable tumour mass invading the lumbar vertebrae was identified. In 1977 she developed bony metastases in the occipital and upper thoracic region which were treated with local radiotherapy. Over the next few years she developed further metastases within the axial skeleton, confirmed both on technetium pertechnetate and MIBG scanning. She was treated with therapeutic doses of iodine 131 MIBG in 1985 and 1987 because of progressive skeletal metastases with some symptomatic relief. In 1989 the patient developed right shoulder and foot pain and was noted to have further metastases within the right upper ribs, dorsal spine and metatarsals. These were treated with local radiotherapy with good response. Recently in May 1990, the patient experienced pain in her right upper humerus. Radiographs confirmed a lytic metastasis (Fig. 4) which was treated with local radiotherapy. Despite the presence of extensive metastases, the patient carries on with a normal working life, her blood pressure being well controlled on labetolol.

Discussion

The skeletal system is the most common site for phaeochromocytoma metastases. In Lynn et al's series (1986), 38 patients out of 56 with metastatic phaeochromocytoma had bone metastases with an average interval from diagnosis of primary phaeochromocytoma to discovery of bone lesions of 6.5 years (range 0–20 years). This is in accordance with our two cases presenting with bone metastases 4 and 14 years after initial diagnosis. Several case reports have shown that survivals of 5–20 years are not uncommon (Engleman & Sjoerdsma, 1964; Traub & Rosenfield, 1970; James et al, 1972). Of our two patients one is still alive after 17 years while the other patient recently died 23 years after presentation, confirming that malignant phaeochromocytoma may be slow growing. Prolonged survival is probably due to more aggressive treatment of hypertension with adrenergic blocking agents. James et al (1972) and Lynn et al (1986) have shown that the axial skeleton is the most common site for bone metastases. Although these are classically expansile and lytic, bone metastases from phaeochromocytoma may have a variable appearance, including mixed-sclerotic on radiographs. In the skull vault a metastasis may be easily confused with a haemangioma. The importance of considering a metastasis in the differential diagnosis of a bony lesion in patients with phaeochromocytoma is therefore emphasized. Similarly, histologically phaeochromocytoma may be confused with a large variety of neoplasms. In our first case, although the initial histology on the femoral lesion was reported as lymphoma, review showed it to be a metastatic phaeochromocytoma deposit. Hasegawa et al (1989) emphasized this in their case where a metastatic phaeochromocytoma deposit was initially misdiagnosed as metastatic renal cell carcinoma.

In conclusion, patients with malignant phaeochromocytoma may develop bone metastases very late and can survive with metastatic disease for many years.

Acknowledgments

We would like to thank Miss Michelle Robinson for typing the manuscript and Mr Seamus Griffin for preparing the illustrations.

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Computed tomography of lesser sac hernia through the gastrohepatic omentum

By *T. L. Tran, MB BS, FRCS, FRCR, F. Regan, MB BS, MRCP and M. A. O. Al-Kutoubi, MD, DMRD, FRCR

Department of Radiology, St Mary's Hospital, Praed Street, London W2 1NY, UK

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Keywords: Computed tomography, Gastrointestinal tract, Internal hernia, Lesser sac, Gastrohepatic omentum

Internal hernia is an unusual cause of intestinal obstruction and pre-operative diagnosis on plain films has seldom been made. Before the introduction of computed tomography (CT), the literature on the subject was composed principally of case reports, often based on observations made at surgery or autopsy. However, with the increasing use of CT, pre-operative diagnosis of paraduodenal hernias has been made (Passas et al, 1986; Day et al, 1988). We report a case of lesser sac hernia through a rare congenital defect in the gastrohepatic omentum. The diagnosis, based on the findings of CT, was made pre-operatively. The CT appearance of the condition has not been described in the literature previously.

Case report

A previously healthy 24-year-old female presented with a 6-hour history of epigastric colicky abdominal pain and clear vomiting. She was apyrexial and normotensive with a pulse rate of 90/min. Her abdomen was not distended but was tender with guarding in the epigastric region. Initial laboratory findings included a leucocytosis of 13 000, normal serum biochemistry and serum amylase. Supine and erect abdominal radiographs

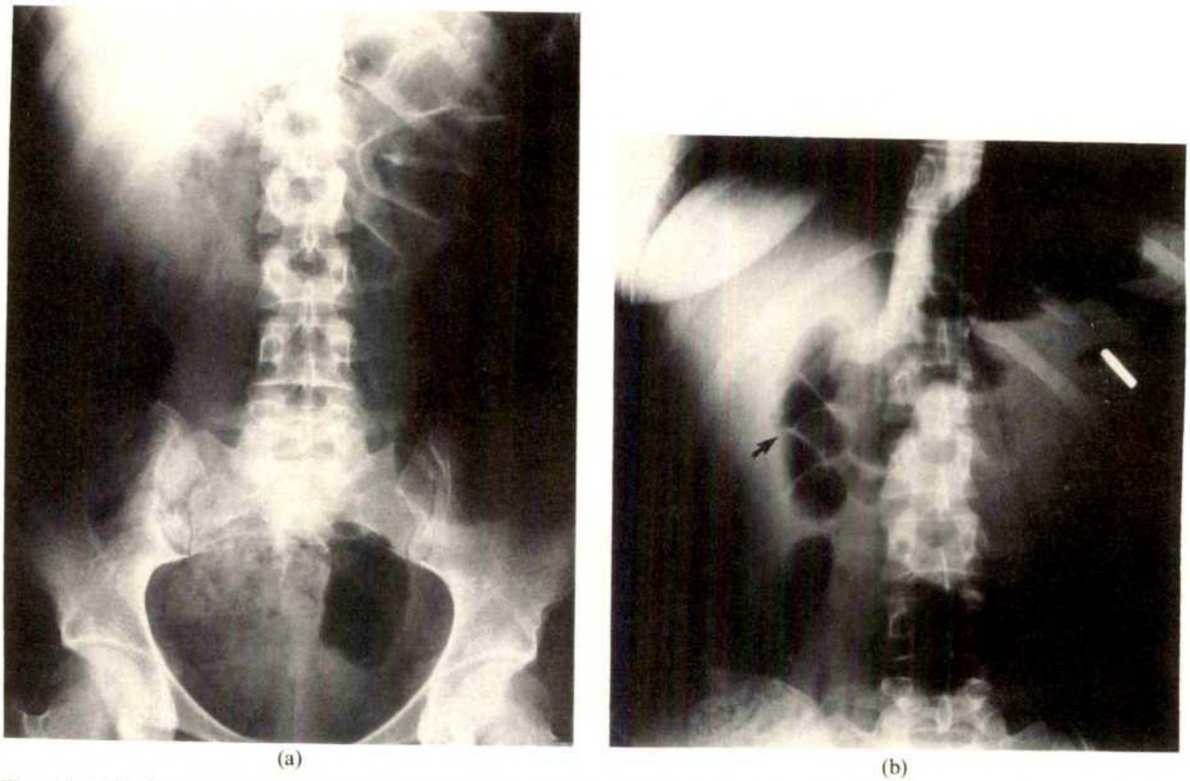
(a) (b)

Figure 1. (a) Supine and (b) erect abdominal radiographs on admission, demonstrating a circumscribed collection of dilated loops of small bowel in the lesser sac, compressing and displacing the stomach laterally. The large arrow shows small bowel loops ascending and descending towards the hepatorenal fossa before herniating into the lesser sac. Note that the signs of intestinal obstruction in the abdominal area below the lesser sac are minimal despite complete obstruction of the hernia.

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*Author for correspondence.

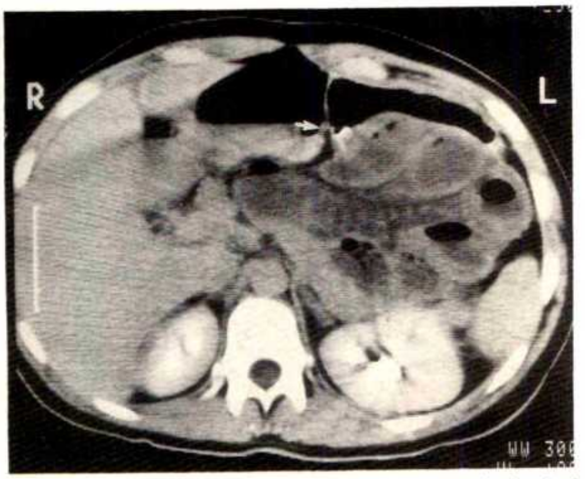

Figure 2. Computed tomograph of the abdomen at the level of the foramen of Winslow demonstrating loops of small bowl with thickened walls in the lesser sac. The stomach with the nasogastric tube *in situ* is displaced anteriorly. The splenic flexure and the descending colon are compressed and displaced. Note that anterior to the portal triad which form the anterior edge of the foramen of Winslow, there are loops of small bowel which are continuous with the small bowel in the lesser sac, thus allowing possible differentiation of hernia through the gastrohepatic omentum from hernia through the foramen of Winslow. The congenital defect in the gastrohepatic omentum is the area extending from the lesser curvature of the stomach (arrow) to the portal triad.

(Fig. 1) on admission revealed a circumscribed collection of dilated loops of small bowel in the upper abdomen medial to the stomach shadow which was also noted to be moderately distended. In accordance with the clinical diagnosis of small bowel obstruction, she was treated with intravenous fluid and nasogastric tube suction.

The following day, her abdominal symptoms remained unresolved. Abdominal radiographs were repeated which revealed no change in the appearance of the dilated small bowel loops in the upper abdomen. Serum amylase was repeated and found to be elevated at 534 units/l. A diatrizoate meglumine–diatrizoate sodium (gastrografin) meal and follow-through was performed. A 30 minute film demonstrated compression of the gastric outlet and the lesser curvature by the dilated small bowel loops, and no contrast medium was seen distal to the pylorus. The appearances were thought to be due to ileus, probably due to acute pancreatitis. Abdominal CT was performed as an emergency.

Computed tomography demonstrated the small bowel loops with thickened walls sandwiched between the stomach and the retroperitoneal structures: the pancreas and the left kidney which form the posterior wall of the lesser sac (Fig. 2). The stomach with the nasogastric tube *in situ* was displaced anteriorly. The splenic flexure and descending colon were compressed and displaced posterolaterally. A diagnosis of lesser sac hernia was made. The abdominal radiographs were reviewed and herniation through the foramen of Winslow was thought to be the most likely cause.

At surgery, 125 cm of jejunum had herniated through a defect in the gastrohepatic omentum just medial to the portal triad, measuring 4 cm in diameter. The bowel was gangrenous and the proximal viable margin was only 30 cm from the duodeno-jejunal junction. The bowel was resected and the defect was closed. She made an uneventful recovery and has been asymptomatic since her discharge from hospital.

Discussion

Internal hernias constitute only 1% of all intraperitoneal causes of intestinal obstruction. In the majority, herniation occurs through one of the peritoneal recesses, the commonest being the paraduodenal fossa, representing 53% of all internal hernias (Hansmann & Morton, 1939). Herniation into the lesser sac may occur through one of the following structures: the foramen of Winslow, the transverse mesocolon, the greater omentum or the gastrohepatic omentum (Stewart, 1962). The commonest method is through the foramen of Winslow, constituting 8% of all internal hernias (Hansmann & Morton, 1939). Herniation through a primary opening in the gastrohepatic omentum is exceedingly rare, the only published case was that of Gants and Ryle (1953).

Defects in the gastrohepatic omentum, through which herniation occurs, can be congenital or acquired. Of the acquired type, both surgical and blunt abdominal trauma have been implicated. In the case described by Gants and Ryle (1953), the defect was probably secondary to crush injury sustained 3 years previously, and through which herniation of the greater omentum and transverse colon occurred with resultant partial volvulus of the stomach. The gastrohepatic omental defect in our case was probably congenital since there was no previous history of any abdominal trauma or operation and the margins of the defect were smooth and well formed with no adhesions in the periphery.

The predisposing causes of internal herniation through the gastrohepatic omentum are unknown. In our case, the event was spontaneous with no apparent cause found in the patient's history or at surgery. Nonetheless, the majority of internal hernias result from congenital anomalies of intestinal rotation and peritoneal attachments (Pennel & Shaffner, 1971). The gastrohepatic omentum is normally shielded by the liver in the hepatorenal fossa. Access of viscus to the hepatorenal fossa is facilitated when the greater omentum is atrophic and loops of intestine are rendered mobile due to abnormally long mesentery (Erskine, 1967). It is possible that alteration in intra-abdominal pressure including parturition, vomiting and straining may provoke the onset of internal herniation in those patients with an anatomical predisposition (Erskine, 1967).

The radiographic appearances of intestine in the lesser sac may be characteristic and when correctly interpreted could lead to the diagnosis (Stewart, 1962). The essential findings are a circumscribed collection of loops of gas-containing intestine in the upper abdomen medial and posterior to the stomach, associated with mechanical intestinal obstruction. The stomach is usually displaced anteriorly and to the left side with extrinsic pressure on the lesser curvature. In our case, the appearances on the abdominal radiographs were characteristic but misinterpreted.

The exact nature of the gas collection may be difficult to interpret; this problem can be overcome by aspirating the stomach with a nasogastric tube and then repeating the film, obtaining in addition a lateral view preferably in an erect position. Distinction from other conditions which can present with gas in the lesser sac, such as perforated gastric ulcer or abscess, is possible by identification of the presence of a mucosal pattern and fluid levels within the herniated bowel. If the findings are still equivocal, valuable information can usually be gained by barium studies of the gastrointestinal tract when clinical condition allows. A soluble contrast meal was performed in our case but was unhelpful as the contrast medium could not pass beyond the gastric outlet which was completely obstructed by the herniated intestine.

Computed tomography provides excellent delineation of the structures forming the boundaries of the lesser sac. In the case described and illustrated here, CT clearly demonstrated the small bowel loops in the lesser sac, allowing a confident diagnosis pre-operatively (Fig. 2). Computed tomography is helpful in elucidating the nature of the gas collection in the lesser sac, especially when the radiographic findings are uncharacteristic. It is also helpful in differentiating a true hernia from other conditions such as abscess and perforated viscus which may present with gas in the lesser sac. In the event of a hernia, the fluid levels are confined to the intestinal loops and do not conform to the anatomical recesses of the lesser sac. Other structures such as greater omentum and gall bladder, which have been found in the lesser sac after herniating through the foramen of Winslow (Erskine, 1967), are more readily demonstrated on CT than on plain radiographs. Paraduodenal hernias, in particular those on the left side, may present with a circumscribed collection of loops of bowel in the left upper abdomen indenting the posterior wall of the stomach. Computed tomography can differentiate these from a lesser sac hernia by demonstrating the retroperitoneal position of the herniated intestine behind and to the left of the body of the pancreas (Passes et al, 1986). It may also demonstrate a loop of bowel interposed between the stomach and the body of the pancreas due to the duodeno-jejunal flexure which is antero-medially displaced by the herniated intestine (Day et al, 1988).

In our case, owing to the obstruction of the gastric outlet, the signs of intestinal obstruction in the abdominal area below the lesser sac were minimal (Fig. 1). A loop of small bowel ascending towards the hepatorenal fossa before joining the herniated intestine could also be identified; this had led to the initial misdiagnosis of hernia through the foramen of Winslow. Erskine (1967) reviewed the literature on lesser sac hernia through the foramen of Winslow and found a number of these patients had demonstrated these radiographic features. The obstruction of the gastric outlet is due to either the loop of bowel passing across the duodenum before herniating into the lesser sac or the intestinal loops at the hernial ring, therefore air will not pass down into the intestine, and typical signs of obstruction are either absent or minimal even though the intestine in the hernia is completely obstructed. Our case has also demonstrated that hernia through the gastrohepatic omentum can not be differentiated from hernia through the foramen of Winslow on plain films but CT may be able to do this by demonstrating intestinal loops anterior to the foramen of Winslow before joining the intestine in the lesser sac (Fig. 2). The defect in the gastrohepatic omentum can, in retrospect, be seen on the CT images as the area extending from the lesser curvature of the stomach to the portal triad.

In summary, when dealing with patients with acute abdomen, the possibility of the condition should be kept in mind and, with careful interpretation of the radiology, pre-operative diagnosis can be made. The plain radiographic findings could be characteristic and diagnostic. However, when the radiographic findings are equivocal and barium studies are unhelpful or contraindicated, CT may readily provide the diagnosis.

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1991, *The British Journal of Radiology*, 64, 375–376

Case of the month

Not so pseudo

By Charles J. Wakeley, BSc, FRCS, FRCSEd, Victor N. Cassar-Pullicino, DMRD, FRCR and Iain W. McCall, DMRD, FRCR

Department of Diagnostic Imaging, Robert Jones & Agnes Hunt Orthopaedic Hospital, Oswestry, Shropshire

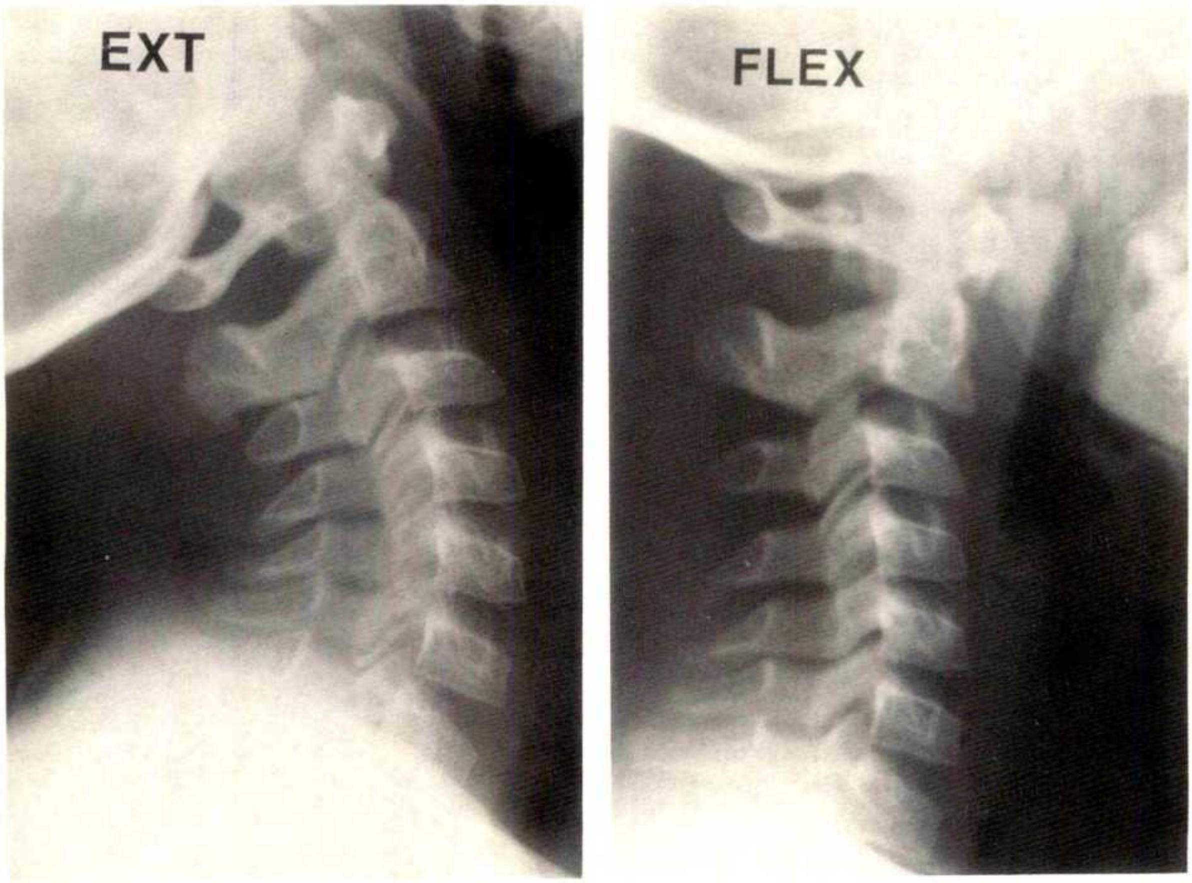
(*Received January 1990*)

Keywords: Spinal injury, Cervical spine, Pseudosubluxation

A 9-year-old boy presented in the Casualty Department complaining of a painful neck. The previous night his brother had jumped on his head causing forced flexion of his cervical spine. The patient had restricted active and passive neck movements without neurological symptoms or signs. Figure 1 shows lateral views in flexion and extension of his cervical spine on admission to hospital.

Describe the radiological appearances. What is your diagnosis?

Address correspondence to Dr V. N. Cassar-Pullicino, Department of Diagnostic Imaging, The Robert Jones & Agnes Hunt Orthopeadic Hospital, Oswestry, Shropshire SY10 7AG.



(a) (b)

Figure 1. Flexion and extension lateral radiographs of the cervical spine.

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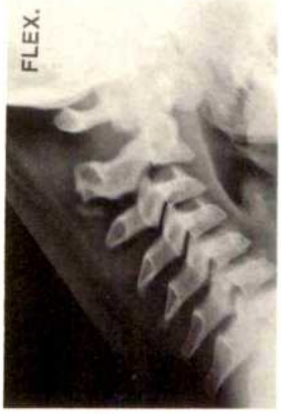

Figure 2.

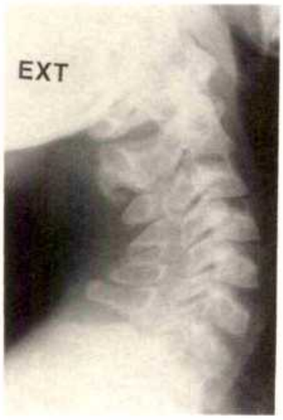

Figure 3.

Figure 2. Flexion lateral view of the cervical spine. Pseudosubluxation of C2/C3 with intact posterior cervical line. New bone formation in the interspinous space at C2/C3.

Figure 3. Post-traumatic new bone formation and incorporation with spinous process of C2.

The radiological features are consistent with physiological C2/3 pseudosubluxation. Rapid resolution of his neck pain allowed the patient's early return home. A month later, the radiographic appearances were unchanged and the patient was entirely asymptomatic, participating fully in sports activities including heading footballs! He remained symptom-free with a normal range of neck movements, but radiographs 3 months later showed soft tissue ossification in the supraspinous and interspinous ligaments between C2 and C3, indicating healing of posterior ligamentous trauma (Fig. 2). Although the degree of C2/C3 angulation and subluxation were within the accepted normal range, this patient clearly sustained disruption of the posterior ligamentous complex at the same level.

Discussion

Physiological anterior displacement of C2 on C3 in children is a well recognized feature; its misinterpretation in some cases has led to prolonged and unnecessary treatment. This phenomenon is most commonly encountered prior to the age of 8 years (Townsend & Rowe, 1952; Jacobson & Bleecker, 1959). The frequency and degree of displacement diminishes with age, and most authors report an upper age limit of 14 (Cattell & Filtzer, 1965; Swischuk, 1977). A few cases, however, have occurred between 17 and 21 years of age (Harrison et al, 1980). The main fulcrum for motion of the cervical spine in the sagittal plane is at the C2/C3 level in children and the C5/6 level in adults. Apart from the anterior wedging of the upper cervical vertebral bodies and the horizontal alignment of the apophyseal joints normally present at this level, the hyper-mobility has been ascribed to the increased ligamentous laxity associated with under-development of neck musculature in the young. On flexion, the posterior arch of C2 moves forward with the body of C2 and, in so doing, aligns itself in a straight line fashion with the posterior arches of C1 and C3. This alignment is normal and constitutes the basis of the posterior cervical line (Swischuk, 1977). The posterior cervical junction will pass through (or less than 1 mm in front of) the anterior cortex of the spinolaminal line of C2, indicating normal stability at this segment. This helpful line is currently used to distinguish physiological from pathological anterior displacement and is seen to be normal in our case.

The degree of normal motion through the C2/C3 apophyseal joints between full flexion and full extension can be striking with a "step-off" of up to 4 mm (Swischuk, 1977). The underlying factors that predispose to the physiological C2/C3 variant must also make this level the most vulnerable in a forced flexion injury and predispose to posterior ligamentous disruption. The presence of ligamentous ossification in this patient indicates that serious injury was sustained to the posterior osteoligamentous complex of C2 and C3, and false comfort was derived from the radiographic criteria discussed above. Posterior ligamentous damage is serious, predisposing to spinal instability. The previous literature on C2/C3 pseudosubluxation has been notable by the minimal radiographic follow-up, which was deemed unnecessary in view of the asymptomatic state of the patients. Given a history of trauma, our case indicates that the presence of pseudosubluxation should not be taken as synonymous with absence of any significant injury, and children with injuries to the neck should be treated symptomatically for whatever soft tissue injury that may be present, despite the presence of pseudosubluxation. Radiographic evidence of increased ossification and incorporation with the C2 spinous process removed any need for surgical intervention (Fig. 3) in this case.

Acknowledgments

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1991, *The British Journal of Radiology*, 64, 377–378

Book reviews

Urologic Pathology with Clinical and Radiologic Correlations. Ed. by A. Someren, pp. xi + 755, 1990 (Pergamon Press Inc., Oxford), £76.00.
ISBN 0-02-413750-2

As its title suggests, this multi-author text, written by 28 pathologists, radiologists and urologists from the Emory University School of Medicine in Atlanta, Georgia, seeks a multidisciplinary approach to urological pathology.

The book is divided into seven chapters, with varying numbers of contributors to each, covering urological kidney disease, the urinary passages, renal transplantation, the prostate and seminal vesicles, the testis and paratesticular structures, the penis and scrotum, and the adrenals. Each chapter is preceded by a table of topics covered, and starts with sections on normal development and structure, radiological evaluation, specimen preparation and developmental anomalies.

The text is well laid out in double columns and the system of headings and subheadings is easy to follow, although there are a few minor irritations such as the occasional misquoted reference, typographic error (clump kidney, p. 26, aneurysuis, Fig. 1-97) and transposition of figure captions (Fig. 4-48 for 4-49).

For pathologists, the coverage of all aspects of urological pathology, including newer techniques such as fine needle aspiration cytology, is excellent, and I found no important entities that were not included. Sections such as those on tumour pathology and renal transplantation are particularly good, and packed with useful practical information. In general, the text is as up to date as could be reasonably expected in a multi-author volume addressing a rapidly developing subject.

The book is lavishly illustrated with black and white pictures. The radiographs, ultrasonograms, computed tomography (CT) and magnetic resonance imaging (MRI) scans are excellent, but a proportion of the photographs of gross specimens and some of the photomicrographs are dark and have lost detail in their reproduction. This is a pity since, in general, they have been well chosen to illustrate the entity under discussion.

As a pathology text, this book compares well with other recent publications in the field such as Murphy's *Urological Pathology*, although the standard of the pathological illustrations in the latter are often better. However, the strength of the present work lies in the careful correlation of the radiological and pathological aspects of urological disease. The advent of modern imaging techniques has rendered many of the more subtle aspects of gross morphology, traditionally the province of the histopathologist and morbid anatomist, to be readily apparent to the radiologist examining the intact patient. This has had an obvious impact in terms of more accurate diagnosis, and a more rational approach to clinical management, but requires a pooling of knowledge and experience from radiologists, clinicians and pathologists.

This book clearly, and, in my view, very successfully follows this "team" approach to urological diseases. It is to be highly recommended to pathologists who seek and active role in the investigation and management of patients, and to radiologists who require a better understanding of the pathological entities with which they deal. Urologists will acquire from this book a comprehensive guidance as to how their colleagues, in the investigative specialties, can help them in the diagnosis and management of their patients.

The book is very reasonably priced, at a level to make it accessible for personal use by specialists in the field. It should certainly find a place in all pathological, radiological and urological departmental libraries.

R. A. Risdon

Procedures in Gastrointestinal Radiology. Ed. by J. Dobranowski, D. A. Stringer, S. Somers and G. W. Stevenson, pp. xiii + 231, 1990 (Springer-Verlag, Berlin), DM 190.
ISBN 0-387-97113-0

The purpose of this book is to provide a detailed step-by-step description of the various examinations in gastrointestinal radiology, with emphasis on barium studies that provide the most useful and accurate clinical information. Endoscopic procedures are also described in the hope that this will allow for a closer interaction between radiology and endoscopy. It is aimed at radiology residents as well as being a reference for practising radiologists.

The first half of the book is primarily concerned with the upper gastrointestinal tract, small bowel and large bowel contrast studies. One of the problems with describing barium examinations is that radiologists differ considerably in their techniques of performing double contrast and small bowel studies. The authors describe a fairly rigid regime, both for double contrast barium meal and for the double contrast enema, being particular in the number and sequence of films taken. For radiologists embarking on barium studies the description of the small bowel meal is quite easy to follow. However, the description of examining the double contrast barium enema technique is confused by several line drawings subdividing the convolutions of the sigmoid into five distinct subtypes. The description of the double contrast barium meal is, however, well illustrated with both radiographs and line drawings. Cross-sectional diagrams help to understand the three dimensional anatomy of the stomach and duodenum and the postural manoeuvres carried out during the double contrast barium study.

The chapter on the small bowel describes both the dedicated small bowel study and the small bowel enema as well as the per-oral pneumocolon and reflux small bowel enemas. Unfortunately the continuing debate about the role of the small bowel meal versus the small bowel enema is to a great extent overlooked. There are sections devoted to contrast examinations in the immediate post-operative situation, in the assessment of fistulas and late post-operative assessment of patients. Defaecography is also well described.

There is a large section of the book on paediatric gastrointestinal examinations including extensive description of ultrasound examination in children; this partly reflects the major interest of one of the authors. However, the value of ultrasound in examining the gastrointestinal tract in the adult seems to have been ignored. The section on biliary procedures includes techniques of percutaneous liver biopsy and transjugular liver biopsy; techniques which are probably carried out by very few radiologists. Oral cholecystography and operative and post-operative cholangiography are mentioned but intravenous cholangiography, which although very rarely carried out these days, does not receive any mention at all.

The techniques of endoscopy are apparently included in this text since these authors are amongst those radiologists who perform endoscopic procedures. Most radiologists in training would omit these sections when reading through the book. The short section on pharmacological agents used in gastrointestinal studies is helpful.

In general the book is well laid out and easy to read and is excellently illustrated with radiography and line drawings. An appendix list barium products, other contrast agents and catheters which have been mentioned in the book. Unfortunately many of these are not recognizable as being available in the U.K. The book is relatively expensive, although it is no designed to carry in one's pocket. It would be a valuable text in any training department and may fill the gap which has been left by Laufer's *Double Contrast Gastrointestinal Radiology*, now being out of print.

A. Grundy

Invasive Investigation of the Heart; a Guide to Cardiac Catheterization and Related Procedures. By Graham Miller, pp. xiv + 496, 1989 (Blackwell Scientific Publications, Oxford), £79.50.
ISBN 0-632-02027-X

Despite considerable developments in non-invasive imaging, invasive procedures still play a central role in investigation of cardiac disease and in particular in coronary artery disease. This text book concentrates on cardiac catherization and cardiac angiography and as the preface states is "addressed to cardiologists undertaking catheterization procedures in the hope that a description of the various procedures will be of use in helping them to develop the necessary skills". It is largely written by Dr Graham Miller who was for many years in charge of the cardiac catheterization laboratory at the Brompton Hospital. As would be expected it is a very practical book. Though it concentrates on adult cardiac catheterization it also covers congenital heart disease.

Nearly half of this book is on techniques with chapters on equipment (catheters and other devices), right and left heart catheterization techniques as well as catheter manipulation. There are several non-angiographic chapters including measurement of pressure and of oxygenation, calculations in catheterization, oxygen consumption and indicator dilution techniques. There are clear and practical descriptions supplemented by a good selection of diagrams. Quantitative angiography is covered in some depth but there is only a brief chapter on complications. A chapter on interventional techniques gives a good grounding on this wide ranging topic but I would have liked to have seen a little more caution expressed when embolization techniques are described. A short account of angiographic equipment and techniques seems a little dated with details of a film changed but no mention of digital cardiac angiography.

The remainder of the book looks at catheterization in specific disorders. There are good and full accounts of coronary arteriography, valvular heart disease as well as myocardial and pericardial disorders. There is a comprehensive and useful diagrammatic atlas of congenital coronary anomalies at the end of the dealing with coronary angioplasty. Pulmonary angiography and aortography are briefly covered. As stated by the principal author there has been no attempt to comprehensively cover congenital heart disease, but the basic principles are detailed and there is a useful angiographic atlas section demonstrating normal anatomy as well as a range of most of the abnormalities. There is a useful separate chapter dealing with congenital heart disease in the adult. Finally, there are chapters on management of cardiovascular emergencies in the ITU, electrophysiology and pacing and the role of catheterization in heart/lung transplants.

This book is well laid out with each chapter being clearly divided into sections. There are plentiful illustrations of equipment and techniques with good clear diagrams. The angiographic plates which have a matt finish are well chosen and of good quality.

Overall this book is an excellent practical guide to cardiac catheterization and cardiac angiography. I think it will become an essential text for cardiologists in training and where radiologists are actively involved in cardiac catheterization, this will be a valuable bench book to have or to have available in the department library.

J. F. Reidy

NMR in Biomedicine: the Physical Basis. Key Papers in Physics. Ed. by Eiichi Fukushima, pp. viii + 167, 1989 (American Institute of Physics, New York), £22.00.
ISBN 0-88318-609-B

This book is essentially a reprinted collection of papers that contribute towards the physical basis of nuclear magnetic resonance (NMR) as used in biomedicine. The editor has selected 17 papers which he divides into three categories. The first is entitled "General, Historical" and includes classic pa-pers published between 1946 (Bloch on nuclear induction) and 1966 (Ernst and Anderson on Fourier transform NMR). This is followed by "Instrumentation and Technique" which includes, for example, the paper by Hoult and Richards on the signal to noise ratio of the NMR experiment. The final category is "RF Field Effects on Biological Samples", starting with the 1978 paper by Bottomley and Andrew and continuing with a number of papers on inductive and dielectric losses in biological systems, and on coil design.

Inevitably the book contains a lot of fascinating material and is a good read. It is a better read than one would achieve by carrying around a loose-leaf folder containing photocopies of the 17 original articles. But by how much? I was disappointed by the cursory editorial comments that were provided; an average of just three to four lines for each article. I would have enjoyed these articles so much more if they had been accompanied by a more extensive account of the prevailing scientific and technical background, their impact at the time of publication etc. For example, how abruptly were the "floodgates for Fourier transform NMR" opened by the paper of Ernst and Anderson? To what extent are the predictions of Bottomley and Andrew borne out in practice?

The overall utility of this book should perhaps be judged not only by what it includes but also by what it misses out. In the preface the editor specifies that he has omitted some major areas of NMR (e.g. imaging) as well as the most recent papers. I find the omission of original papers on imaging techniques particularly disappointing and somewhat surprising. They may, in due course, by included in a complementary collection of papers, however, I would have much preferred to see them in this volume, possibly as additions to the existing articles, possible as replacements for some of the articles in the latter sections of the book.

The main appeal of this book will be to physicists and technologists who wish to gain a further appreciation of the principles and historical content of biomedical NMR. More generally, this collection of reprints will serve to emphasize to all of those in the biomedical NMR community that so many of the techniques and recent developments relating to NMR in biomedicine are based on ideas and experiments that were published in the early days of NMR.

D. Gadian

BIR Bulletin

Honorary Editor, BIR Bulletin: D. Rickards, LRCP, MRCS, FFR(D)SA, FRCR
Please address all correspondence to: Honorary Editor, BIR Bulletin, The British Institute of Radiology,
36 Portland Place, London W1N 4AT
The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

Radiology & Oncology '91

Brighton, 29 April - 1 May 1991

Med X Ray Preview

49th BIR Annual Congress

This year the BIR Annual Congress, Radiology & Oncology 91, will be held at the Metropole Hotel in historical Brighton.

As reported in the March BIR Bulletin, the Congress Scientific Programme has been carefully put together to be of maximum interest and benefit to members. Delegates have the choice of attending four parallel sessions for the duration of the congress and five on Monday 29 April.

MED X RAY, now well established as the UK's largest technical exhibition associated with the radiological sciences, will again take place in conjunction with the Annual Congress. The Brighton exhibition will be the fourth MED X RAY exhibition to be jointly organized by the BIR and the College of Radiographers, whose conference will also take place at the Metropole Hotel at the same time. Over 75 companies have reserved space to date and a number of new products will be on display this year covering all aspects of radiology and radiotherapy.

AGFA-GEVAERT Ltd will be showing their new Matrix CR520 and Matrix Cr2030 cameras. BRUEL & KJAER (UK) Ltd will be introducing their new ultrasound system 3535, a general purpose ultrasound scanner for B- and M-mode scanning and audio, FFT and DFM Doppler studies. ELSINCT will be showing their Gyrex view a new joint MRI/CT workstation and FUJI PHOTOFILM Ltd will be displaying two new computed radiography products.

KODAK LTD have a whole range of new products on display covering video, mammography, film processing and silver recovery and LOKAS LTD will be showing a new silver recovery system which is described as being pollution control efficient. PHOTOSOL Ltd will have a new fume measurement system on display and PHILIPS will be showing their new BV 29, an advanced mobile and surgical interventional imaging system. 3M will be displaying their new laser imager 'XL' system and SIEMENS will be showing their products 'Somatom AR' for CT and 'Magnetom P8' for magnetic resonance. The CALUMET COACH COMPANY are the only company to date to have booked a mobile exhibit. They will be bringing along a fully operational Mobile MR imaging centre which will be on show in Hall 5.

With all that will be on display, we anticipate that delegates will wish to spend much time in MED X RAY. Free tea and coffee will be available throughout the day to delegates and light snacks at very competitive prices will also be available at the designated refreshment areas placed at points within the exhibition halls.

We look forward to seeing you in Brighton!

VANESSA WHITEHEAD
CONFERENCE MANAGER

Radiology History Committee Report 1989–1990

Professor I. Isherwood, Chairman
Dr J. M. Guy, Honorary Secretary
Mr G. Mountford, Honorary Treasurer

This committee is an independent body representing five professional organizations associated with radiology, in alphabetical order: the British Institute of Radiology, the College of Radiographers, the Institute of Physical Science in Medicine, the Royal College of Radiologists and the Radiology Section of the Royal Society of Medicine. As well as representatives chosen by these organizations, the committee includes individuals with a strong interest in the history of radiology and has co-opted members with professional skills relating to libraries, museums and document archives.

A year ago, the committee achieved its first aim, which was to encourage the parent organizations to arrange a single joint conference during 1995. This is to be the major scientific event of the year, and will include an academic programme relating to the history of radiology. The technical exhibition is also to have a significant historical element, celebrating the British contribution to the science of radiology since Rontgen's discovery of X-rays in 1895. The Centenary Congress will be held in the new Birmingham Conference Centre from 12th to 16th June 1995.

Partly to assist in the setting up of this exhibition, but also to provide a continuing and powerful research tool, the committee wishes to set up a database recording the location of equipment and documents radio-historical, wherever they are to be found in Britain.

Our January meeting was held in the Science Museum store, where we were able to see the wealth of material which the museum is able to store but is not able to have on permanent display. As a result of this visit, members were convinced that it would be a mistake to raise funds to duplicate this large holding of radiological apparatus, while acknowledging that there is a case for local collections elsewhere in the country. Instead we shall offer advice to assure the continued survival of existing historical apparatus. Since its foundation, the members of the committee generally and Dr Adrian Thomas in particular, have been corresponding with radiographers, radiologists, physicists and engineers who have information or apparatus relating to the history of radiology.

Until very recently, the committee lacked any of the funds necessary to set up a historical database or provide the expenses of volunteers working "in the field". However, in August of this year the committee received a very generous anonymous donation which will provide the nucleus of the necessary finance. Part of the donation will be used to purchase a share in the computer which is about to be installed in the BIR. A much larger sum is needed to provide a salary for the organizer of the project and the other running costs.

Can we make a strong appeal for donations to assist in its work, from industry, from grant-aiding bodies and from all individuals working in the broad field of radiological science and practice? British radiology has a valuable heritage. This is your heritage. Help us to rescue and preserve it.

European Congress of Radiology

Members of the BIR who are interested in attending the European Congress of Radiology to be held in Vienna, Austria, on 15–20 September 1991 may like to know that the organizers of the travel and accommodation will be pleased to arrange for an all inclusive price for flight and accommodation based on travelling and returning to Manchester Airport. This is additional to the departure points listed in the Congress brochures.

For further information contact the organizers of travel and accommodation: Reiseburo Mondial GesmbH, Faulmanngasse 4, A-1040 Vienna, Austria, Tel. (+43) 1 58 804-0, Fax (+43) 1 569 185. Further information may be obtained from Dr A. E. Hugh, Tel. (0782) 662333.

Roger Berry awarded Order of St John

Dr Roger Berry, President of the BIR 1986–1987, has been admitted as an Officer (Brother) of the Order of St John.

The Order of St John dates back to the Crusades. Its motto is,"In the service of mankind", and it is responsible for the St John Ambulance Brigade as well as the maintenance of the Hospital for Eye Diseases in Jerusalem.

Dr Berry, Director of Health, Safety and Environmental Protection at BNFL, attended an investiture in London on 7 February when he was presented with a medal, although he was actually awarded the Order of St John last summer.

He is retiring as the Captain responsible for medical training in the Royal Naval Reserve and will miss the duties, which involved visiting and inspecting naval reserve establishments on a regular basis.

NPL Dosimetry Standards and Calibration Services

Radiotherapy Standards Users' Meeting
National Physical Laboratory, 13 December 1990

Consistent measurements and traceability to primary standards at the National Physical Laboratory were the main themes of this first meeting organized for customers and users of its calibration and measurement services for X-rays, gamma-rays and electron-beams. The meeting was attended by 47 participants, each from a different institution.

The morning session, chaired by Mr A. DuSautoy, was devoted to formal presentations by NPL dosimetry Branch staff covering many aspects of the present services offered to hospital radiotherapy departments and other organizations. Mr C. J. Moretti began the session by describing the administrative procedures involved in the calibration for a customer from the initial inquiry to the return of the instrument and the despatch of the NPL certificate. It was explained that calibrations were undertaken during two fixed periods of the year in order to reduce both the overall charge to the customer and the time taken to perform the calibration for all customers. Mr B. Owen then discussed the NPL absorbed dose to water calibration service for high energy X-rays and 60 Co gamma-rays. The 1983 and 1990 Codes of Practice were compared and it was demonstrated that the new service and recent Code of Practice gave results in better agreement with other national codes, and, more importantly, did so with a reduced uncertainty. Dr M. J. Rossiter briefly described the service offered to radiology departments for the determination of generating potential, based on the calibration of penetrameters and kVp meters. Dr P. H. G. Sharpe reviewed the present position in chemical dosimetry with particular emphasis upon the use of Fricke dosimetry for the determination of absorbed dose to water. He also discussed ongoing work aimed at launching a new service to cover the dose range from 10 Gy to 20 kGy based on the determination of the free radical concentration in small alanine pellets using electron spin resonance spectroscopy. It was hoped to extend the low dose limit to about 1 Gy within the next 2 years. Finally, Mr C. J. Moretti gave three short presentations on (a) therapy-level secondary standards, (b) a possible extension to the services offered by NPL to include calibrations for diagnostic and mammographic X-ray qualities, and (c) the effects upon customer calibrations arising from proposals to extend and improve the present buildings and facilities within the next year to 18 months.

The afternoon session, chaired by Dr J. B. Hunt, was an open discussion of points raised by the participants themselves. Much of the discussion was devoted to the recently launched high-energy photon absorbed dose to water calibration service and the associated 1990 IPSM Code of Practice. It was agreed that the 1990 Code of Practice and the NPL calibration service are an improvement on the 1983 Code of Practice and an NPL calibration at 2 MV. The apparent 60 Co/4 MV calibration factor difference was noted, as was the observed spread in the 60 Co calibration factor of about 1%; NPL was urged to continue to try to solve these problems. The correction arising from the fact that the effective point of measurement of a cylindrical ionization chamber is not coincident with the geometric centre was deliberated, and it was agreed that the magnitude of the appropriate correction was small: less than 0.3% over calibration distances ranging from 80 to 150 cm. The need for NPL to provide calibrations for both diagnostic radiology and mammography in X-ray beams similar in quality to those routinely used in practice was mentioned, and NPL agreed to continue its dialogue with the IPSM Diagnostic Topic Group over the next year in order to finalize proposals for such an improvement in its present facilities and services.

At the end of the meeting, participants were given a guided tour of the laboratories and facilities. The tour included visits to the therapy-level exposure rooms, the NPL Linac exposure room where high-energy absorbed dose to water calibrations are carried out, the chemical dosimetry laboratories, including both solid and liquid dosimetry systems, the protection-level exposure room and the computer room, where theoretical aspects of radiation dosimetry are developed and applied to improve the primary standards. Many participants took the opportunity to develop further the discussions started earlier in the day.

The introduction to this type of meeting was welcomed by the participants, and, as a result, it is planned to hold the next one in about 18 months time.

Julian Hunt
Alan DuSautoy

Library News

Library Cataloguing Project

I was commissioned by the BIR to catalogue the entire book-stock of the Library and the reserve stock in the basement — approximately 3 000 items — from October 1990 to March 1991. I found this task extremely interesting and challenging, and am very grateful for the on-going advice and support of the Systems Librarian, Stephen Johnson, and part-time Librarian Gunnel Ingham. Initially the project involved completing a computer input form for each book or pamphlet, but since the end of January, when the new computer system was installed with the requisite peripherals and 'CALM' (Computer Assisted Library Management), details can be input directly onto a VDU screen. We have all found the 'CALM' package amazingly versatile, flexible and sophisticated. In fact we have very few criticisms of this in-house integrated system. Only a small amount of customization will be required.

Already more than 900 records have been entered into the disc memory. There are fields in each record for the title of the work, subtitle, series statement (important for such publications as conference proceedings, European and international congresses, etc.) up to eight authors or editors, publisher, place of publication, date of publication, three physical dimensions (width x height x depth in centimetres), pagination. Additional fields are used to show the nature of the work, such as whether it contains an index, glossaries, illustration, diagrams, tables, graphs, equations, plans, algorithms, circuit diagrams, appendices, etc., price, whether hardback or paperback, edition, shelf spine-label classmark, ISBN/ISSN. A large abstract/notes field is also attached to each record, in which other data-elements can be included at the discretion of the Librarian. Eventually a controlled-vocabulary thesaurus will be developed (I have already generated a manual card-index list of about 500 terms) with carefully devised interrelationships between the terms, such as narrower terms, equivalent terms, broader terms and 'see' terms. From this thesaurus, keywords will be allocated to each book. We envisage that the average number of such keywords per book will be around 15, but there is room in the computer memory for up to 54 words or terms per item.

When the cataloguing project is completed, it will be possible to search under any of the aforementioned data-elements and all books in the library fulfilling the search criteria will be selected out in a separate memory. This listing can then be alphabetically sorted and printed out for Library users. Boolean logic search parameters can be created, using the controlled language thesaurus or natural language. Because the computer and software are of the 4th generation variety, search-times are in the order of split seconds rather than the several minutes that used to be the case with older systems, even when searching thousands of records, literally character by character.

The in-house classification system is in the process of being expanded and refined to take account both of future information needs of clients and the plethora of new developments, advances and techniques which are manifesting themselves in the various branches of Radiology. Section B (Radiation Physics) and Section C (Radiation Protection) have already been revised, and over the next 3 months, Gunnel will be inviting specialists to the Library who will advise us on the revision of the remaining sections: A (General); AA (Quality Assurance); D (Radiobiology); E (Diagnostic Radiology); F (Radiotherapy and Oncology); G (Nuclear Medicine); H (Ultrasound); J (Computed Tomography); and K (Nuclear Magnetic Resonance). If you feel that you may be able to assist in these revisions we would love to hear from you!

PETER J. VINCETT

Recent additions to the library

BRAGG, D. G. et al (Eds), 1990. Yearbook of Diagnostic Radiology.

GOZZETTI, G. et al (Eds), 1989. Intraoperative Ultrasonography in Hepato-biliary and Pancreatic Surgery. A Practical Guide.

LEVINE, M. S., 1989. Radiology of the Oesophagus.

ROSENBERGER, A., ADLER, O. B. & TROUPIN, R. H., 1987. Trauma Imaging in the Thorax and Abdomen.

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays and Thursdays).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

There is an agreement which allows limited use of the RSM library for reference purposes, including photocopying and searches.

Members should apply to the BIR librarian for a visitors card.

BIR Calendar

Unless otherwise indicated, enquiries about the following events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-580 4085).

RADIOLOGY AND ONCOLOGY 91 and MED X RAY
29 April–1 May
Metropole Hotel, Brighton
Speakers:

3M Mayneord Memorial Lecture:
Prof. D. M. Goldenberg
Silvanus Thompson Memorial Lecture:
Dr R. Berry
Presidential Address:
Prof. C. A. Joslin
Mackenzie Davidson Memorial Lecture:
Prof. S. Dische

Radiation Oncology and Radiobiology: Particle Therapy
June 7, 1991
Organizer: Dr R. D. Errington
Speakers: Dr D. Bewley, Dr N. McNally, Prof. G. W. Griffin, Mr J. Hungerford, Dr T. Bates, Dr S. Gore and Prof. J. M. Slater

The New Legislation — Friend or Foe (After the White Paper ... and into Europe)
June 13, 1991
Scientific Lecture Theatre
All day meeting organized by the Industry Committee
Chairmen: Prof. C. A. Joslin, Dr O. Craig and Miss D. Rigg
Speakers include Dr J. Roylance, Dr I. Watt, Mr E. Sutherland, Prof. I. Isherwood, Mrs S. Williams and Mr P. Richardson

Conversazione
June 27, 1991
Painter's Hall, London
Lecture: "Half an Eye on the Sky", by Sir Stephen Furness.

New BIR Members

Medical

Dr Gian Thomas **Abbott**, MB, ChB, MRCP
Liverpool, Diagnostic Radiologist
Dr R. A. **Allan**, MA, MRCP
London, Diagnostic Radiologist
Prof. Venkataramanan **Balasundaram**, MB, BS, FRCS, DMRT,FRCR
Longfield, Kent, Radiotherapist/Oncologist
Dr Arpan **Banerjee**, MB, BS, MRCP, FRCR (Part I)
London, Diagnostic Radiologist
Dr Kaushik-Kumar B. **Bhagat**, MB, ChB, FRCS
London, Diagnostic Radiologist
Dr Graham R. **Cherryman**, MB ChB, FRCR
Nottingham, Diagnostic Radiologist
Dr Lanil W. **de Silva**, BSc, MB, BS, FRCS
London, Diagnostic Radiologist
Dr Duncan F. **Ettles**, MB, ChB, MRCP
Bristol, Diagnostic Radiologist
Dr Joanna J. **Fairhurst**, MA, MRCP, FRCR
Southampton, Diagnostic Radiologist
Dr Emma **Friedman**, MB, BS, MRCP
London, Diagnostic Radiologist
Dr J. M. **Geurts**, Radiologist
Belgium, Diagnostic Radiologist
Dr Anand P. **Gupta**, BSc, MB, BS, DMRE
Kenya, Diagnostic Radiologist
Dr George G. **Hartnell**, BSc, MB, ChB, MRCP, FRCR
USA, Diagnostic Radiologist
Dr Susan J. **Hotston**, MB, ChB, MRCP, FRCR
Clwyd, Diagnostic Radiologist
Dr John **Hynes**, MB, BCh, MRCP
Manchester, Diagnostic Radiologist
Dr Kenneth **Ibe-Lamberts**, MB, BS,Part I FWACS & FMCR
Nigeria, Diagnostic Radiologist
Dr Gabriel **Lamb**, MB, ChB, DMRD, FRCR
Liverpool, Diagnostic Radiologist
Dr Kim Shang **Lee**, MB, BS
London, Radiotherapist/Oncologist
Dr Eric J. **Loveday**, MB, BS, MRCP, FRCR (Part I)
London, Diagnostic Radiologist
Dr Paul N. **Malcolm**, MB, BS, BSc, MRCP
London, Diagnostic Radiologist
Dr John M. **McGovern**
Belfast, Diagnostic Radiologist
Dr Tarik F. **Massoud**, MB, BCh, BAO, LRCPI
Oxford, Diagnostic Radiologist
Dr Alan M. **Norris**, MRCPI, MRCP
Manchester, Diagnostic Radiologist
Dr Peter W. **Ratcliffe**, MSc, MB, BS, DMRD
London, Diagnostic Radiologist
Prof. Yasuhito **Sasaki**
Japan, Nuclear Physician
Dr David J. **Widdowson**, MA, MB, BS, DMRD, FRCR
Clwyd, Diagnostic Radiologist
Dr Marie **Wilkins**, MB, BCh, FRCR (Part I)
New Malden, Surrey, Radiotherapist/Oncologist

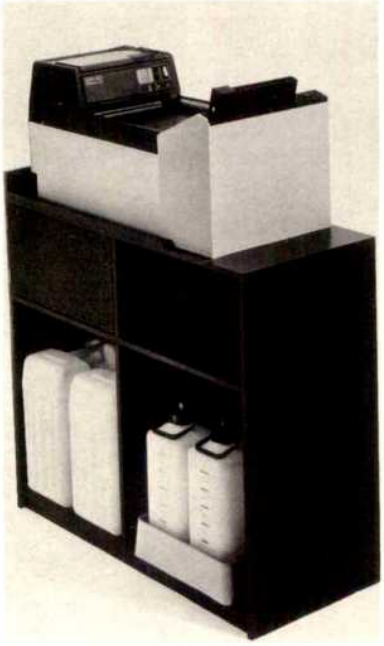
Non-Medical

Mr Anthony **Flynn**, BSc, MSc
Leeds, Physicist
Mr Peter **Draycon**, BSc (Hons) Chemistry
Dunstable, Beds, Meadox (UK) Ltd
Mr Nicholas J. **Dudley**, BSc, MSc, MIPSM
Lincoln, Physicist
Dr Francis R. **Hudson**, BSc, PhD, C Phys,FInstP
London, Physicist
Dr Andrew P. **Jones**, BSc, MSc, MIPSM
Manchester, Physicist
Ms Verlee **Kirkness**, MAIR
Australia, Radiographer
Mr James **Nol**, Radiologic Technologist
Australia,Radiographer
Mrs Maria **Paphiti-Dimitriadi**, BSc, MSc
Greece, Physicist
Mrs Simone **Plaut**, HDCR(R), DCR(R), FETC
London, Radiographer
Mr Gordon T. **Ryan**, FAIR, FCR
Australia, Radiographer
Mr Peter **Spencer**, DCR CT
Leighton Buzzard, Beds, CEA UK Ltd
Mr Christopher **Varian**, HDCR, Dip M, MCIM
Bracknell, Berks, 3M Ltd
Mr Phillip J. **Supple**
Camberley, Surrey, Calumet Coach Co Ltd

Industry News

Specialist Medical Film Processing from IGP

IGP has a range of automatic processors which can reduce patient exposure to X-rays. As well as the DURR MED 260 and DUUR MED 430 processors for mammography and high throughput, respectively, new products include an XR35 processor, which can process 35 x 43 cm chest X-ray films, an XR20 dental processor for all dental films and the IGP Silver-matic, which recovers more silver from processors than previous units and virtually eliminates discharge of toxic silver into the environment.



For more information contact Keith M. Whiffin, IGP (UK) Ltd, 1-5 Cutler's Road, South Woodham Ferrers, Chelmsford, Essex CM3 5JS .
Tel. 0245 323555 .
Fax. 0245 323762.

Advances in Cancer Imaging and Therapy: Theme of Mayneord Lecture

The 8th BIR/3M Mayneord Memorial Lecture, supported by the 3M Medical Imaging Systems Group, will be given during Radiology and Oncology '91, in the Oxford Room at the Metropole Hotel, Brighton. It is scheduled for 12.15 pm on Tuesday, 30th April.

The lecture, "New Advances in Cancer Imaging and Therapy with Radio Labelled Anti-bodies", will be delivered by Professor David M. Goldenberg from the Centre For Molecular Medicine and Immunology at Newark, New Jersey, USA.

The award, which includes a £250 honorarium and a commemorative plaque of honour, is made annually to an individual who has made a major contribution in the field of radiology. It is named after the late Professor W. V. Mayneord, CBE, who was President and Honorary Member of the British Institute of Radiology.

Applications are already being invited by the President of the BIR for the 9th lecture to be given next year.

For further information contact Chris Varian, Medical Imaging Systems Group, 3M United Kingdom plc, 3M House, PO Box 1, Bracknell, Berkshire RG12 1JU. Tel. 0344 58799.

Success in US Trials for Kontron Sigma 44

Kontron Instruments' ultrasound system, the Sigma 44 High Velocity Colour Doppler, which uses advanced Quasar (quantitative unaliased speed algorithm recognition) technology, has been at the centre of studies carried out by a Research Group at the University of Alabama.

In *in vitro* and clinical trials, the group compared a commercially available colour Doppler imaging system with the Kontron Sigma 44 and concluded that Kontron's patented Quasar technology "appears to have the potential of using colour Doppler to measure high flow velocity as accurately as continuous-wave Doppler."

The Group found the Sigma 44 capable of recording velocities higher than those found in even the most abnormal blood flow seem in clinical practice. According to Kontron, the Quasar technique allows the detection of blood flow velocities more than three times greater than conventional un-aliased velocity in both directions. This the company sees as a significant advance in CFM real-time direct quantitative investigation of physiopathological blood speeds.

Quasar was developed by Kontron to maximize on the many advantages of colour Doppler while overcoming the problems associated with its inherently low Nyquist limit which results in signal aliasing. The technology uses two "colour flow mappers" operating simultaneously at different frequencies. The phase shifts produced by these frequencies are compared and their difference used to produce a much lower beat frequency. This allows a large increase in the Nyquist limit and eliminates aliasing.

Modular in concept, the Sigma 44 is designed with the latest electronic architecture, has full IBM compatibility and can be easily connected with standard MS-DOS peripherals or into a patient database management system.

For further information please contact Drew Mowatt, Kontron Instruments, Blackmoor Lane, Croxley Centre, Watford, Herts WD1 8XQ. Tel. 0923 245991. Fax. 0923 50146.

Second Generation Computed Sonography Takes Ultrasound into the 1990s

Acuson's 128XP uses a 128-channel, software optimized system to produce images with excellent resolution and colour Doppler performance. One of many new features is Vector Array which allows the system to steer ultrasound lines in any direction while originating those lines from any point on the transducer face. This results in a larger near field of view without compromise to resolution and colour Doppler sensitivity and allows access to anatomic regions that larger formats cannot reach.

Another capability of the system is High Performance Curved Array, which uses the powerful image formation of the XP platform and new transducer technology to overcome the far field degradation and image artifacts common with conventional curved linear transducers. It is particularly beneficial for large near field studies, such as examining large liver tumours.

For further information contact David James, Acuson Limited, Wiltron House, Rutherford Close, Stevenage, Herts SG1 2EF. Tel. 0438 740066
Fax. 0438 365166.

Lecture, Conference and Meeting Facilities

Available for use at 36 Portland Place, London W1
The BIR Lecture Theatre, with raked seating and extensive audiovisual equipment, accommodates 100 people in air conditioned comfort.

The conference room accommodates a maximum of 34 people with modular furniture which can be arranged to suit the needs of individual users.

For further information please contact the House Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

Creo Optical Tape Drive Now Available

The world's first commercially available optical tape drive, the Creo 1003, and the drive technology itself are to be marketed in Europe by ICI Imagedata. The Creo 1003 uses optical tape media to store 1 terabyte (1000 gigabytes) of data on a single 12 inch tape reel. It is now possible to store the equivalent of 5 000 magnetic tape cartridges on just one reel of ICI's 1012 optical tape at a very low media cost with no risk of accidental erasure and an archival life of 15 years. Creo has now begun commercial production of the model 1003 and units will be available for delivery later in 1991.

For further information contact David Bennett, ICI Imagedata.
Tel. +44 707 323400.
Fax. +44 707 337896

High Definition Sonography from Dornier

Dornier Medizintechnik recently launched their version of the Acoustic Imaging AI 3200 Scanner which has already been enthusiastically received in the USA. The new system has a high degree of software control, allowing for upgrading to be completed in seconds, and is able to store up to 64 images in the hard disk. Dornier has perfected solid state probes right from 3.5 to 10 MHz which have not been available before on electronic scanners. The efficiencies in transducer design allows users to re-assess their choice of transducer for it is quite normal with this new system to use 5.0 MHz or 7.5MHz for general scanning thanks to the "multi-frequency" wide band technology employed and new development in the transducer lens and backing materials.

Dornier of West Germany acquired Acoustic Imaging last year bringing the benefits of AI's transducer expertise alongside their already thriving Lithotripsy technology.

For further information contact Geoff Faulkner, Dornier Medizintechnik,
P O Box 1182, Chippenham, Wiltshire SN15 1ZA.

BIR

Conference Services

Is there a seminar, conference or evening get-together you want to organize, but you don't have the time? The BIR Conference Office may be able to help you. Please call Vanessa Whitehead, Conference Manager, to discuss possibilities.

BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £275 p.a. member companies are offered an attractive benefits package.

To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex
TW8 9AX.
Tel. 081-560 2131. Product Areas 1. Contact
Mr G. Mountford, Director.

American Medical Ltd
PO Box 971, London SW10.
Tel. 071-352 8051. Fax: 071-376 4508.
Product areas 1, 3, 4, 5, 7, 8.
Contact Betsy Riley, Managing Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury,
Bucks HP20 2TP.
Tel. 0296 395222.
Product areas 4, 5, 6.
Contact Mr James McLaughlin, Sales and
Marketing Manager.

Bard Ltd
Forest Houe, Brighton Road, Crawley,
West Sussex RH 11 9BP.
Tel. 0293 27888, ext. 2204.
Product area 2.
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Assurance of Quality in the Diagnostic X-Ray Department

The report of the BIR Diagnostic Methods Committee

Editors
J A Garrett, Director of Medical Equipment Management Organisation, Bristol & Weston Heath Authority, UK
D Gifford, Deputy Chief Physicist, Frenchay & Southmead Health Authorities, UK
M J Harvey, Middlesex Hospital, London, UK
P Goddard, Consultant Radiologist, Bristol Royal Infirmary, UK

Producing images, whether photographically or in electronic form, is the primary purpose of the diagnostic radiology department.

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The second section of the book presents the wider systems approach to quality assurance with reference to recent standards for QA and how these may be applied to diagnostic radiology.

The final part discusses quality assurance in computer assisted imaging, computed tomography, magnetic resonance imaging, and digital subtraction angiography.

Radiologists, radiographers, physicists and technicians alike will find *Assurance of Quality in the Diagnostic X-Ray Department* both a practical handbook for day-to-day use and a stimulus in developing their understanding of the scope of quality assurance.

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OPTIMIZATION OF IMAGE QUALITY AND PATIENT EXPOSURE IN DIAGNOSTIC RADIOLOGY

(BIR Report 20)

Editors:

B M Moores, B F Wall, H Eriskat and H Schibilla.

Contents: Introduction. Image Perception. Physical Assessment of Image Quality. Clinical Assessment of Image Quality. Optimization of Image Quality and Patient Dose - Paediatric Radiology - Mammography - Chest Radiography - Technical Factors. Patient Dose Measurements and Quality Assurance. CEC Image Quality and Exposure Criteria Trial. Panel Discussions. Conclusions and Perspectives for Future Research. CEC Study Group Document on Quality Criteria for Diagnostic Radiographic Images.

Key components in quality assurance in diagnostic radiology are image quality and patient exposure. Quality criteria defining optimum procedures should ensure that the most accurate and reproducible diagnostic information is obtained from radiographs, but at the same time minimize exposure of the patient to ionizing radiation. Formulation of such criteria was the aim of a workshop organized jointly by the CEC and NRPB, of which this book is the edited proceedings. A revised list of quality criteria for common diagnostic examinations was drawn up by a CEC Study Group and is appended to the proceedings.

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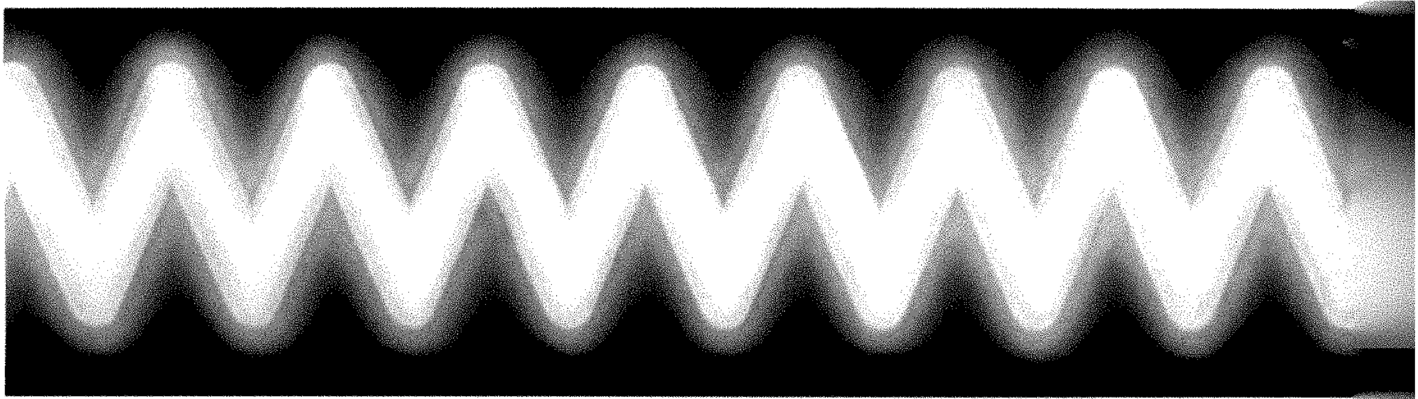

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(BIR Report 19)

Editor

N J McNally, Gray Laboratory, Mount Vernon Hospital, Middlesex

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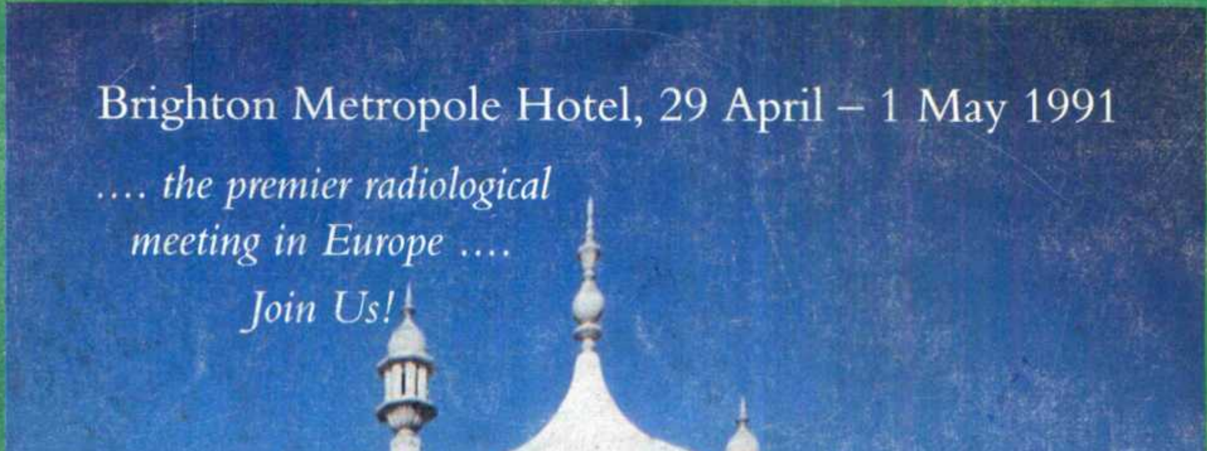

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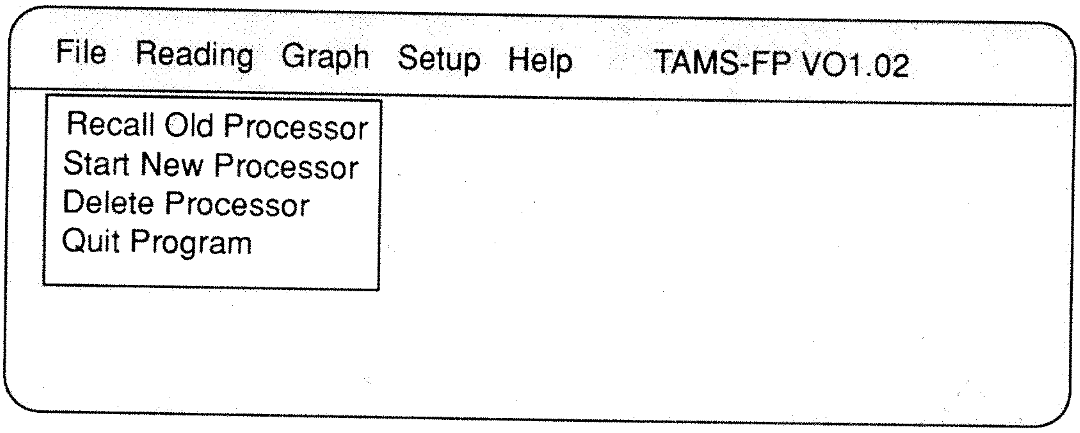

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Hardcover DM 295,– ISBN 3-540-19622-6

This new edition describes the most recent developments and techniques practiced at the Christie Hospital in Manchester. The Manchester school of thought is renowned worldwide as a leader in radiotherapy.

From the reviews of the first edition:
"... It should be in the library of every radiotherapy department, and in the hands of every trainee..."

British Medical Journal

H. Pettersson, Lund; **H. Ringertz**, Stockholm

Measurements in Pediatric Radiology

1991. X, 185 pp. 35 figs. Hardcover DM 120,–
ISBN 3-540-19665-X

Normal anatomy and proportions in children may vary during growth and differ considerably from the adult. It is therefore essential, even for the experienced radiologist, to have a standard based on numerous pediatric radiological examinations. With this excellent reference, every pediatric radiologist is equipped with normal values with which to compare and better recognize abnormal measurements.

P. D. Phelps, G. A. S. Lloyd, London

Diagnostic Imaging of the Ear

2nd ed. 1990. XIII, 218 pp. 314 figs.
Hardcover DM 350,– ISBN 3-540-19570-X

A completely updated edition of "Radiology of the Ear", 1983, with coverage of new MRI techniques.

R. D. Rubens, I. Fogelman, London (Eds.)

Bone Metastases

Diagnosis and Treatment

1991. XII, 247 pp. 82 figs. Hardcover DM 156,–
ISBN 3-540-19619-6

Bone Metastases brings together the many recent developments that are gradually improving the prospects for patients with secondary involvement of the skeleton in a primary cancer elsewhere. The book's editors, themselves authorities in the fields of oncology and bone disease respectively, have brought together experts from many disciplines to provide comprehensive coverage of metastatic bone disease.

P. Butler, London (Ed.)

Imaging of the Nervous System

1990. XII, 271 pp. 334 figs.
(Clinical Medicine and the Nervous System)
Hardcover DM 348,– ISBN 3-540-19522-X

This book is designed especially for the resident in one of the clinical neurological specialities; it provides a concise account of the imaging appearances of conditions affecting the neuraxis. The emphasis is mainly on CT and MRI, but duplex ultrasound, digital subtraction angiography and the newer radiopharmaceuticals are not neglected.

Distribution rights for Japan: Igaku Shoin, Tokyo

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MED X RAY — A glimpse of the future

It is reported elsewhere that the President prayed for fine weather at Brighton, to attract delegates to the Congress, and also for inclement weather to assure good attendance at the lectures and the exhibition.

His prayers were answered, as poor weather ensured good attendance at MED X RAY where over 80 companies displayed their products, and were able to demonstrate the need of their specialities in the present climate of the British Health Care Industry.

Last month's BJR contains a report on the RSNA 1990, and states that it was unusual there to see a stand without the ubiquitous computer in some form or other. This also applied to MED X RAY in Brighton this year.

A feature of RSNA in Chicago is the number of mobile units on display with CT, MR, and mammography units installed on board, but only one Company showed such a unit in Brighton. This was the Calumet Coach Company, and much interest was shown in how a fully operational MR unit could be housed in such a vehicle. Lithotripsy and cardiac catheterisation can be incorporated in mobile units made by Calumet.

Laser images and daylight systems were on show by most of the film companies, and in addition, Fuji showed new Computed Radiography systems, which attracted a lot of interest. Processors are now available which complete film processing in under 40 seconds, and Kodak had one of these new units on show.

Philips Medical Systems introduced the new BV29 mobile surgical X-ray unit, on show for the first time in the UK. Also creating a lot of interest was the Platinum ultrasound unit with revolutionary new Colour Velocity Imaging (CVI), as well as equipment from the leading product ranges of CR, MR, PACS, Radiotherapy and Cardiovascular.

Computers were also well in evidence on the major equipment company stands, and most of these companies showed their range of X-ray, CT and MR equipment, as well as Nuclear Medicine and Ultrasound units. There was a special emphasis in some cases on Magnetic Resonance Units, as there is some evidence that a lot of money will be spent on this equipment in the United Kingdom over the next few years.

Oncology has been added to the title of the Congress, as from this year, and it was good to see more products on show to attract the Radiotherapist and BIR members working in Oncology. Siemens introduced two major additions to its range of diagnostic imaging system. The "Somatom AR', for computed tomography, and the "Magnetom P8" for MRI. Both scanners use new concepts in terms of technology and space saving.

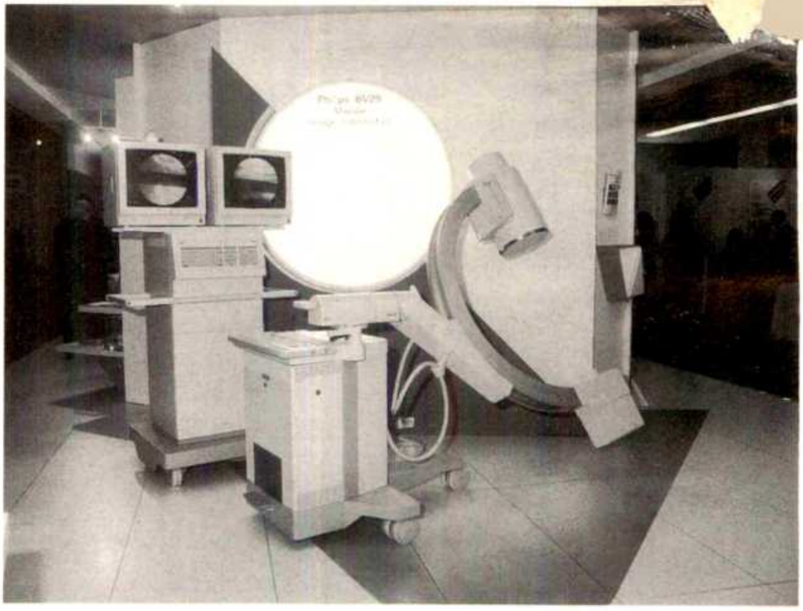
There were a number of Companies at MED X RAY for the first time this year, and we appreciated their comments and enthusiasm. We were also pleased to welcome back one or two companies who were absent in Harrogate last year, so it was good to see a lot of activity on the catheter display stands in Brighton.

Many delegates found time to visit the BIR stand, where sales of ties, mugs, and skeleton T-shirts were on offer. It was heard that a few members drifted to the stand of the College of Radiographers, where sweatshirts and cardigans were on sale, and were in somewhat greater demand, due to the cold and wet weather.

Whatever the delegate could want for imaging or oncology seemed to be on display at MED X RAY, and if he or she felt they needed more study on any subject, the bookstalls of Granta Books, Lippincott and Wisepress seemed able to offer it to them.

We hope that all the Companies displaying their wares in Brighton considered it worthwhile, and that they will be back next year in Birmingham (18-20 May 1992).

GRAHAME MOUNTFORD



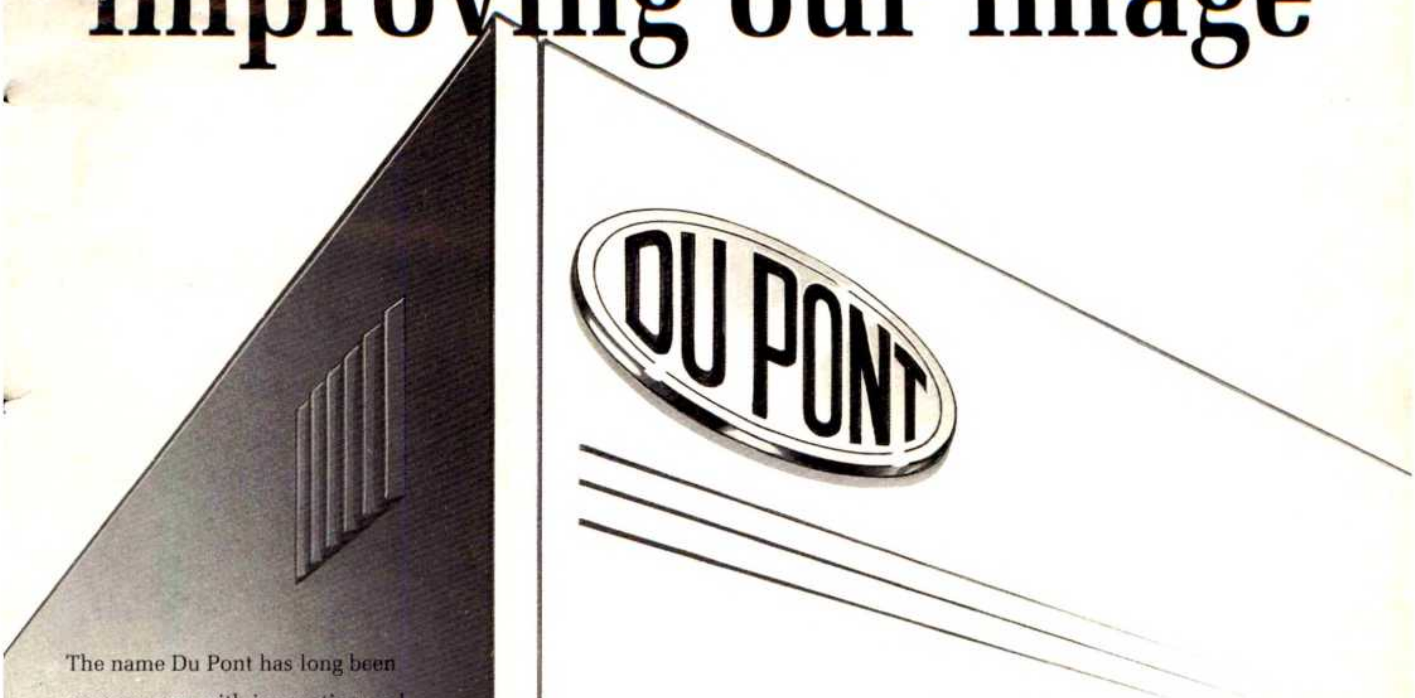
Platinum ultrasound unit with new Colour Velocity Imaging (CVI) (TM).

Musical Evening at the Royal Pavilion

Over one hundred delegates and partners at Radiology & Oncology 91 had a very enjoyable time at the Royal Pavilion, Brighton at the Musical Evening, generously supported by Schering Health Care Ltd. An extremely interesting tour was given of the Pavilion by its resident guide. Starting in the now fully restored Music Room with its rich red and gold wall paintings, the tour moved through the Great Kitchen with its decorative copper canopies and automatic spit and then on to the Banqueting Room where the string quartet had set up. The Banqueting Room was added to the Pavilion by John Nash and was designed to be as spectacular as possible for George's dinner guests. The room has a magnificent central lamp approximately nine metres high and weighing one ton with a silvered dragon carved at its head. One of the most important collections of Regency silver-gilt on public view is displayed on the central table in this room. The string quartet played both modern and classical pieces expertly and the buffet served was superb. The Royal Pavilion provided a delightfully different venue and all who attended had a very enjoyable evening. Thanks was expressed to Schering Health Care Limited for their generous sponsorship of the evening.

Guests admire the elaborate ceiling of the Banqueting Hall

We've spent years improving our image

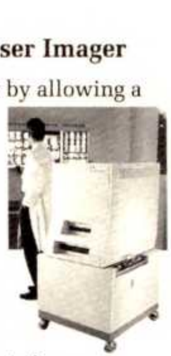


The name Du Pont has long been synonymous with innovation and environmental concern in imaging technology. These technological advances have always been aimed at improving image quality for better diagnoses, and nowhere is this more evident than in the latest Du Pont introductions.

New CRONEX*10S film and Quanta Screen combinations allow faster film speeds to reduce the patient's exposure to radiation, while retaining the high degree of image quality necessary for effective diagnoses.

Daylight Processing was introduced to the U.K. by Du Pont twenty years ago, and since that time a programme of continuous development has led to faster processing times and new, low-fume chemicals to improve the working environment.

The new LINX* Laser Imager improves productivity by allowing a single operator to interface between various electronic imaging modalities – such as CT, MR, DSA and ultrasound – and the film processor. A stationary film transport system that reduces microbanding and user-specific, programmable film densities mean that image quality as well as viewing clarity are kept at an optimum.



The new LINX* Networking System provides the flexible link between electronic imaging systems and the Laser Imager. Separate local memories keep the system operating in the event of partial close down and allow the operator to store and print out images in any order. This can add up to considerable time saving and increased productivity in the busy Radiology Department.

Reduction in radiation dose, improvement in the working environment and increased productivity are just some of the benefits of today's Du Pont products.

We've spent years of research and development on improving our image, so that you will improve the quality of yours.

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Diagnostic Imaging Department
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Redefining Image Quality

DU PONT

Schering Healthcare Fishing Contest

For the third successive year, thanks to the generosity and support of Schering Healthcare, a light-hearted fishing contest has been held in conjunction with the annual Congress of the British Institute of Radiology. This year the event took place at Lakedown, set in the beautiful rolling folds of the Sussex Weald, near to Rudyard Kipling's old home at Bateman's.

Lakedown Fishery is owned by Roger Daltry, who lives in the Woodland setting immediately above the Lakes, which form a chain of crystal pools down the valley. Fourteen rods participated in the events, and sixteen delegates sat down to an excellend dinner in the evening at an ancient coaching inn set in the village of Burwash – well to be recommended. The fishing took place under a brilliant blue sky with a cold northerly wind, following the coldest night at Lakedown since February, with a heavy frost, all of which constitute bad conditions for trout fishing, and sport was not as brisk as might have been hoped for by those participating. In fact, Roger Daltry came down to the fishing lodge in the evening to talk to the participants, and said that he was sorry that sport had not been any brisker, as the lakes had been specially stocked up for us. The greatest number of offers were experienced by a distinguished newcomer to the sport, whom it is hoped we shall see on future occasions.

The catch was as follows:

DR W SMITH 3 fish for 4 lb 13 oz
DR J TEARE 1 fish for 2 lb 7 oz
DR D HUGHES 1 fish for 2 lb 4 oz
DR S PADLEY 1 fish for 2 lb 4 oz
DR M PADLEY 1 fish for 1 lb 10 oz

A discreet veil will be kept over the names of other, less fortunate anglers, among whom is numbered the writer. The magnificent trophy, again donated by Schering Healthcare, is therefore brought to the West Country where it will be admired by the many sportsmen of the area until the next challenge, to be held in 1992 in conjunction with Radiology and Oncology '92 at the Packington Fishery at Meriden, owned by the Earl of Aylesford.

D GIFFORD

3M/BIR Mayneord Memorial Lecture

To mark the success of the 8th 3M/BIR Mayneord Memorial Lecture 1991, Professor David Goldenberg (centre) was presented with the commemorative Mayneord plaque. Also shown are Ken Roche, General Marketing Manager of the 3M Medical Imaging Systems Group (L) andProfessor C A Joslin, President of the BIR (R).

Professor Goldenberg's lecture was entitled "New Advances in Cancer Imaging and Therapy with Radiolabelled Antibodies." The Professor is based at The Centre for Molecular Medicine in Immunology at Newark, New Jersey, USA.

11
12/92

ATTENTION RADIOLOGISTS

Michael Maisey is Professor of Radiological Sciences in the United Medical and Dental Schools of Guy's and St Thomas's Hospitals. He has extensive experience of teaching and research in the development and evaluation of radiological techniques, and in the provision of radiological services using a wide variety of imaging technologies.

John Hutton is a Senior Research Fellow in the Centre for Health Economics at the University of York. For several years his work has concentrated on the application of economic and social evaluation methods in the assessment of medical technologies.

Guidelines for the EVALUATION OF RADIOLOGICAL TECHNOLOGIES

by ***M. N. Maisey and J. Hutton***

- The need for evaluation
- How to assess the diagnostic accuracy of a test, and its impact on further diagnosis and therapy
- ROC curves and how to use them
- Economic techniques for cost analysis
- Clinical trial design, and errors to avoid
- Clear tables and illustrations
- Glossary of terms
- Bibliography for further reading

March 1991, 28 pages, 210x297mm, ISBN 0 905 74925 1, Illustrated, £13.50.

ORDER FORM

British Institute of Radiology, 36 Portland Place, London W1N 4AT.
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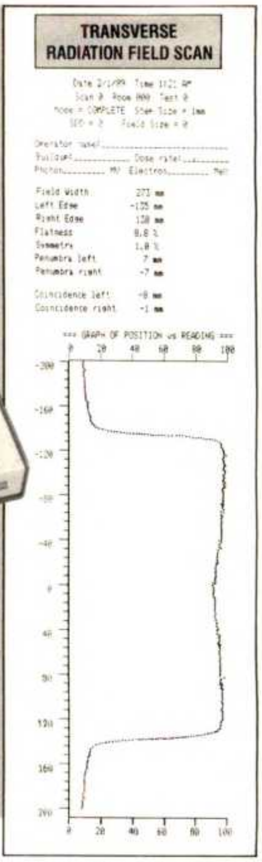
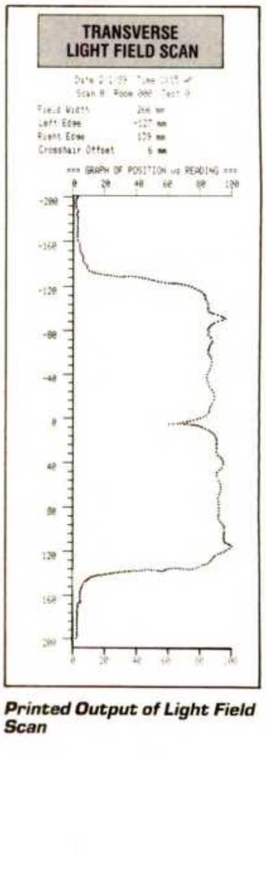


TRANSVERSE RADIATION FIELD SCAN

```
Date 2/1/89  Time 11:21 AM
Scan 0  Room 000  Test 0
Mode = COMPLETE  Step Size = 1mm
SSD = 0   Field Size = 0

Operator name:________________________
Buildup:__________ Dose rate:_________
Photon:________ MV Electron:_______ MeV

Field Width          271 mm
Left Edge           -135 mm
Right Edge           138 mm
Flatness             0.8 %
Symmetry             1.0 %
Penumbra left          7 mm
Penumbra right        -7 mm

Coincidence left      -8 mm
Coincidence right     -1 mm

=== GRAPH OF POSITION vs READING ===
```

Printed Output of Radiation Field Scan



TRANSVERSE LIGHT FIELD SCAN

```
Date 2/1/89  Time 11:15 AM
Scan 0  Room 000  Test 0
Field Width          266 mm
Left Edge           -127 mm
Right Edge           139 mm
Crosshair Offset       6 mm
=== GRAPH OF POSITION vs READING ===
```

Printed Output of Light Field Scan

- Checks light field and radiation field coincidence.
- Analyzes radiation field for flatness, symmetry, and penumbral size.
- Built-in graphics printer provides hardcopy outputs of scan information.
- Single axis diode scanner.
- Self-contained, no cables to attach.

*Developed by Lawrence E. Reinstein, Ph.D.,
Radiation Oncology Department,
State University of New York at Stony Brook.

For more information, request Bulletin 430-14

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RADIOLOGY & ONCOLOGY 91

Brighton 29 April - 1 May 1991

The 49th Annual Congress of the British Institute of Radiology incorporating the joint Spring Meeting with the Royal College of Radiologists and the Radiology Section of the Royal Society of Medicine.

The Scientific programme is organised by the BIR in scientific collaboration with the American College of Radiology.

As an organisation accredited for continuing medical education, the American College of Radiology certifies that this continuing medical educational offering meets the criteria for Category 1 credit for up to 15¼ hours, providing it is completed as designed.

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ORGANISING COMMITTEES

Congress Committee

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Dr G Deutsch	Local Representative
Dr N Garvie	BIR Honorary Secretary
Dr S J Golding	Scientific Programme Chairman
Dr W Hateley	BIR Vice President
Dr M P Law	Scientific Poster Exhibition Chairman and BIR Honorary Secretary
Professor S Lillicrap	BIR Vice President
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Dr N J McNally	BIR Vice President and Honorary Editor
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Mr J Twydle	MED X RAY Advisor
Ms V Whitehead	BIR Conference Manager
Ms M-A Piggott	BIR General Secretary
Dr T Hogan	BIR Publications Manager

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Dr N Garvie
Dr W Hateley
Professor C A F Joslin
Dr M P Law
Professor S Lillicrap
Dr N J McNally
Dr H Nunnerly (RSM)
Dr D Stoker (RCR)
Mr J Twydle
Ms V Whitehead

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Mr A M Oxley and team
RAD Magazine, Kingsmoor Publications
Schering Health Care Ltd
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RADIOLOGY & ONCOLOGY 92

International Convention Centre, Birmingham 18-20 May 1992
British Institute of Radiology 50th Annual Conference

Incorporating the joint Spring Provincial Meeting with the Royal College of Radiologists and the Radiology section of the Royal Society of Medicine.

Radiology & Oncology 92 will incorporate all aspects of modern radiology for all those concerned with diagnostic radiology and radiotherapy.

Proffered abstracts are invited for oral and poster presentations and will form a major element of the meeting.
Deadline for receipt of abstracts: **THURSDAY OCTOBER 31, 1991.**

MESSAGE FROM THE PRESIDENT

Thank you for participating in Radiology & Oncology 91 and the MED X RAY exhibition.

The Scientific Programme Committee, chaired by Stephen Golding, have provided an interesting and stimulating programme designed to bring together practising professionals, to share experiences and exchange information to help provide for the best practices in Radiology & Oncology. I see these activities as a major ongoing function of our large multidisciplinary Institute.

We are especially honoured by having three outstanding speakers for the eponymous lectures and bid them a special welcome. The programme also includes teach-ins and work-in-progress sessions. We hope the mix will prove to be to your satisfaction and invite you to let us know of your views following the meeting.

We again have a splendid MED X RAY exhibition and hope you will make the maximum use of the opportunity to exchange views and discuss the latest developments with your industry colleagues.

I also wish you a most enjoyable time socially, meeting old friends and making new ones. Vanessa Whitehead and the Conference team have been dedicated to preparing for this Congress, and will be found at the Registration desk to help with any queries you may have.

Thank you for joining us. I wish you a successful and enjoyable meeting.

CHARLES JOSLIN

GENERAL INFORMATION

Congress Site

Radiology and Oncology 91 takes place at the Metropole Hotel in Brighton. Plenary lectures are held in the Oxford Room; all other sessions take place as shown on the timetable grid (see pages xi, xii & xiii). A layout map of the hotel is included on the back cover.

Registration

Your delegate's pack contains all relevant tickets (please check these), list of delegates, the MED X RAY handbook and your Congress badge.

Your badge entitles you to admission to all lectures at Radiology & Oncology 91 and to MED X RAY for the days on which you are registered and *must be worn throughout the Congress.*

Registration Desk Opening Times

The registration desk will be situated in the Sussex Lounge and will be open at the following times:

Sunday	4.00pm - 8.00pm
Monday	8.00am - 4.30pm
Tuesday	8.00am - 4.30pm
Wednesday	8.00am - 2.00pm

MED X RAY

MED X RAY runs for the three days of the Congress, from Monday 29 April - Wednesday 1 May, to span the annual meeting of both the British Institute of Radiology and the College of Radiographers. MED X RAY is sited in exhibition halls 3, 7 & 8 of the Metropole Hotel. The opening times are:

Monday 29 and Tuesday 30 April 9.00am - 5.30pm
Wednesday 1 May 9.00am - 4.30pm

Full details of the companies exhibiting are given in the MED X RAY handbook.

Messages

Please check the notice board by the registration desk for messages.

Scientific Poster Exhibition

The large scientific poster exhibition is in the Cambridge Room. Opening times are as for MED X RAY.

BIR posters will be discussed in chaired sessions and a note of the date, time and session of oral presentation will be on the poster. Abstracts are included within the relevant sessions. The BIR poster exhibition includes presentations on the following topics:

Ultrasound
Nuclear Medicine
Interventional Radiology
Nuclear Magnetic Resonance
Computed Tomography
Radiotherapy and Oncology
Radiobiology
Radiological Physics
Radiation Protection

BIR Information Stand

The BIR Stand will be situated within MED X RAY. Further details in the MED X RAY handbook. BIR staff will be available to discuss any aspect of the Institute's activities. We welcome both members and non-members to come and discover the benefits of membership.

Radiology & Oncology 91 Prize Draw

As last year, the BIR's Industry Committee in conjunction with RAD Magazine have organised a competition for delegates at Radiology & Oncology 91. You could win a bottle of champagne!

Telephone

There will be a telephone manned during Congress registration opening hours for urgent messages: Brighton (0273) 25250.

Refreshments

Free tea and coffee will be available within MED X RAY from Monday to Wednesday. Refreshments will be available throughout the day.

Lunch

Light snacks are available on a cash basis from the refreshment points in MED X RAY and there are pubs and restaurants within walking distance of the Metropole Hotel. There are also licensed bars and restaurants within the hotel.

Accompanying Persons Programme (admission by ticket only)

It may be possible to accept last minute bookings for the following at the registration desk. All tours will depart from the Metropole Hotel by 9.30am and return by 5.00pm. (The tour on Wednesday 1 May will return by 2.30pm).

Monday 29 April, Royal Pavilion and St Mary's Bramber

Our first outing takes us to one of the most beautiful buildings in the United Kingdom, the Royal Pavilion, the famous seaside Palace of King George IV. First built in 1787, the Pavilion was rebuilt from 1815 - 1822 in the Indian style. Furniture and works of art include original pieces lent by Her Majesty The Queen.

St Mary's is one of the most ancient houses of its kind in Britain. The foundations date back to the 12th century, the structure being 15th century. Queen Elizabeth I and Charles II are said to have visited there. The house is officially described as 'one of the most important buildings in the County of Sussex'.

Tuesday 30 April, Chichester and Arundel Castle

Tuesday's excursion takes us on a guided tour around the historic Roman town of Chichester, followed by a tour of Arundel Castle. Arundel Castle, situated in grounds overlooking the River Arun in West Sussex, was built at the end of the 11th century. The original castle was badly damaged during the Civil War, but restored in the 18th and 19th centuries. This magnificent castle contains fine portraits and furniture from the 16th century.

Wednesday 1 May, Lewes - the Castle, Museum, Town Model and Anne of Cleves House

From the battlements of Lewes Castle panoramic views of the town and countryside can be seen. The castle dates back to the 14th century. The museum is housed in a 16th century wool merchants house and displays the progress of Sussex people from earliest beginnings until medieval times. The Town Model reveals Lewes' 1000 year old history. It tells of the fortified Saxon settlement which dictates the layout of present day Lewes, of the Norman Castle which still dominates the town, and the battle of Lewes in 1264. Anne of Cleves House takes its name from Henry VIII's fourth wife. This 15th century building has been added to over the centuries. It contains three furnished rooms which give an impression of life in the house in the 17th and 18th centuries.

Social Programme (admission by ticket only)

It may be possible to obtain tickets from the BIR office.

Sunday:
Radiology & Oncology 91 fishing.
A fishing competition will be held in waters near Brighton. Further details from Mr D Gifford, 239 Badminton Road, Downend, Bristol BS16 6NR. Telephone Bristol (0272) 562974.

Informal Welcome Gathering 6pm - 8pm
This will be held in the Viscount Room at the Metropole Hotel. Meet your fellow delegates, have a drink and pick up your conference folder on Sunday evening so that you can plan your lecture programme in advance. (Free.)

Monday:
Meet the Professor Lunch 1.20pm
(Supported by Nycomed UK Ltd)
Ploughmans lunch and beer/soft drinks will be served.

Annual Dinner 7.30pm for 8.00pm
This will be held at the Metropole Hotel. There will be free seating so guests can choose their own companions. Dress is Black tie/dark suit. Cost, including drinks reception and wine and VAT is £34.50 per person.

Disco 9.00pm - 1.00am
This will be held in the Hewison Hall at the Brighton Centre. Tickets are available from the COR Conference Office, 14 Upper Wimpole Street, London W1M 8BN. Price £5 including VAT.

Tuesday:

Radiology & Oncology 91 golf. 12.30pm
The Radiology Golfing Society's golfing match will be held at the East Sussex Golf Club. More details are available from Dr David Rickards, Middlesex Hospital, Mortimer Street, London W1N 8AA. Telephone: 081-380 9070.

Civic Reception 6.15pm-7.00pm
This will be held in the Hewison Hall at the Brighton Centre. (Free.)

Musical Evening at Brighton Pavilion 7.30pm-10.30pm
(Supported by Schering Health Care)
The BIR is delighted to be able to offer an informal musical evening at Brighton's beautiful Royal Pavilion. A buffet will be served with wine and musical accompaniment will be provided. Price including buffet, wine and VAT is £19.00.

Wine Tasting 6.50pm-11.00pm
This evening at the English Wine Centre, Alfriston, will include a tour of the vineyard, the famous English wine museum and a full supper served in the main wine cellars. Cost, including coach transport to and from the Wine Centre and the Metropole Hotel, meal and wine is £20.00 including VAT.

[All information correct at the time of going to press]

MED X RAY EXHIBITORS

Listed below are the companies booked to exhibit at MED X RAY, the UK's largest exhibition devoted to the radiological sciences. It is held jointly with the College of Radiographers and is open to all delegates at Radiology & Oncology 91 throughout the Congress. This is the ideal opportunity to view the very latest in equipment and services to the whole industry, and to meet the leading manufacturers to discuss how modern technology can help your concern. Further information can be found in your MED X RAY handbook which is in your delegates pack.

Annton Ltd
Agfa Gevaert Ltd (X-ray division)
Bard Ltd
Baron Medical PIMS
Bartec Medical Systems Ltd
Bildsystems
Bioglan Laboratories Ltd
British Institute of Radiology
British Nuclear Fuels plc
Bruel & Kjaer (UK) Ltd
Calumet Coach Company
Cea (UK) Ltd
College of Radiographers
Corinth Medical Services
D C Bayman
Data Med Computer Services
Delladene Ltd
Department of Health Medical Devices Directorate
Diasonics Sonotron Ltd
Du Pont (UK) Ltd
Elscint (GB) Ltd
E Merck Ltd
Europlus
E-Z-EM Ltd
Fuji Photo Film (UK) Ltd
Gammex RMI Ltd
Granta Book Exhibitions
H Miller Graphics
IGE Medical Systems Ltd
IGP
Impex Imaging Systems Ltd
Kodak Ltd (Health Sciences)
Konica (UK) Ltd
Lanmark
Laser Lines Ltd
J. P. Lippincott & Co
Litechnica
Lokas
3M UK plc
MAB Services Ltd
MAS Medical Ltd
Medical X-Ray Supplies Ltd
Mitsui
National Physical Laboratory
National Radiological Protection Board
N E Technology
Nicholas Laboratories Ltd
Norgine Ltd
Nucletron
Nycomed (UK) Ltd
Overseas Medical Supplies
Phoenix Imaging Systems Ltd
Philips Medical Systems
Photosol Ltd
Planmed
Polaroid (UK) Ltd
Polystan
Premise Engineering
Radiatron Components Ltd
Radi Medical Systems
Radiologic Ltd
Radius Health Ltd
Schering Healthcare Ltd
Siel Imaging Equipment Ltd
Siemens plc
Silver Coin Ltd
Smith & Nephew Pharmaceuticals Ltd
Spenco Medical
Toshiba Medical Systems
Varian Ltd
Varian TEM Ltd
Videlcom Ltd
Wardray Products Ltd
Wessex Medical Ltd
William Cook
Wisepress Ltd

[Listing correct at time of going to press]

BIR

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The BIR Members' Room

The British Radiological Library

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Radiographer Radiobiologist Radiochemist
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MON	CLARENCE	BALMORAL	NORFOLK	LANCASTER	DUKES
8.45- 9.00	OPENING - Prof. C A Joslin				
9.00 - 10.15	THE SPINE Invited Review Lecture Intradiscal therapy for the herniated nucleus pulposus in the lumbar spine Dr I McCall, Oswestry	FRACTIONATION IN PALLIATIVE RADIOTHERAPY Invited Review Lecture T'were best t'were done quickly: a guiding principle for palliative radiotherapy Dr T Priestman, Wolverhampton	CONSENSUS WORKSHOP CAN YOUR RADIOLOGY DEPARTMENT	IMAGING IN ONCOLOGY Invited Review Lecture MR of Childhood Tumours, Present applications and future perspectives Dr M Hall-Craggs, London	
	COFFEE IN MED X RAY				
10.45 - 12.00	IMAGING AND THE CHEST Invited Review Lecture High Resolution CT of the Lung: Technical factors and clinical indications Dr A G Wilson, London	TEACH-IN RADIOTHERAPY OF BRAIN TUMOURS Organiser: Dr R Rampling, Glasgow	BE FINANCIALLY VIABLE IN THE WAKE OF THE GOVERNMENT WHITE PAPER Organiser: G DeLacey, London	DIAGNOSTIC WORK IN PROGRESS PAPERS AND POSTERS	INTERVENTIONAL ANGIOGRAPHY
12.15 - 1.15	OXFORD ROOM MACKENZIE DAVIDSON MEMORIAL LECTURE Professor S Dische, Northwood				
	LUNCH IN MED X RAY				
2.30 - 3.45	RADIOLOGICAL HISTORY Invited Review Lectures Professor R Grainger, Sheffield Dr S Webb, Sutton Dr W D Hackmann, Oxford Organiser - Dr J Guy, Yeovil	ARE RADIOTHERAPY MACHINES USER FRIENDLY? Invited Review Lectures A Physicist's view, Mr J B Tuohy, Leeds. A Radiographer's view, Mrs M Granville-White, Nottingham	DOPPLER ULTRASOUND Invited Review Lecture The Current State of Doppler Flow Imaging Professor J Woodcock, Cardiff	TEACH-IN MODERN GYNAECOLOGICAL TREATMENT PLANNING Organiser: Dr R Hunter, Manchester	TECHNIQUES AND TECHNOLOGY IN MAGNETIC RESONANCE
	TEA IN MED X RAY				
4.15 - 5.30	TECHNIQUES AND TECHNOLOGIES DIAGNOSTIC IMAGING Invited Review Lecture Experiences with echo-contrast media Dr P N Burns, Philadelphia	TEACH-IN THE PAEDIATRIC GASTROINTESTINAL TRACT Organisers: Dr H Carty, Liverpool Dr D Shaw, London	ONCOLOGY WORK IN PROGRESS PAPERS AND POSTERS	DIAGNOSTIC WORK IN PROGRESS PAPERS AND POSTERS	

TUES	CLARENCE	BALMORAL	NORFOLK	LANCASTER
9.00 - 10.15	BODY MRI Invited Review Lecture MRI of major mediastinal vessels Professor D Foley, Milwaukee	FRACTIONATION IN RADICAL RADIOTHERAPY Invited Review Lecture Accelerated Fractionation Professor A Horwich, Sutton	MANAGEMENT AND AUDIT IN RADIOLOGY Invited Review Lectures Dr J P Owen, Newcastle-upon-Tyne Dr I T Russell, Aberdeen	THERAPEUTIC USES OF NEW ISOTOPES Invited Review Lectures Dr C A Hoefnagel, Amsterdam Professor D M Ackery, Southampton Dr V J Lewington, Southampton Dr S E M Clarke, London
COFFEE IN MED X RAY				
10.45 - 12.00	THE LIVER Invited Review Lectures Professor A Baert, Leuven, Dr G Plant, Basingstoke	BIOLOGICAL TREATMENT IN ONCOLOGY Invited Review Lecture Professor P Selby, Leeds	CENTRAL NERVOUS SYSTEM Invited Review Lecture A critical approach to selecting patients for MR of the nervous system Dr I Mosely, London	DIAGNOSTIC IMAGING - PROFFERED PRESENTATIONS
12.15 - 1.15	OXFORD ROOM MAYNEORD MEMORIAL LECTURE Professor D M Goldenberg, New Jersey (Sponsored by 3M UK plc)			
LUNCH IN MED X RAY				
2.30 - 3.45	IMAGING IN TRAUMA Invited Review Lecture The impact of the M1 air crash on the radiological services at The Queen's Medical Centre Dr B Preston, Nottingham	LOW OR HIGH DOSE RATE IN BRACHYTHERAPY? Invited Review Lectures Dr R Stout, Manchester Dr I Tureson, Gothenburg	NUCLEAR MEDICINE - GENERAL SESSION Invited Review Lecture Professor P J Ell, London	TEACH-IN RADIOLOGY IN THE MANAGEMENT OF LYMPHOMA Organiser Dr S S Golding, Oxford
TEA IN MED X RAY				
4.15 - 5.30	OXFORD ROOM Silvanus Thompson Memorial Lecture Dr R J Berry, Cumbria			

WED	CLARENCE	BALMORAL	NORFOLK	LANCASTER
8.15- 9.00	BIR AGM (Open to BIR members only)			
9.00 - 10.15	URORADIOLOGY Invited Review Lecture Magnetic Resonance Imaging and specroscopy of the normal and transplant kidney Dr A Dixon, Cambridge	QUALITY ASSURANCE IN RADIOTHERAPY Invited Review Lectures Mrs S Williams, Newcastle-upon-Tyne Dr R G B Evans, Newcastle-upon-Tyne Dr P Williams, Manchester	CARDIO VASCULAR IMAGING Invited Review Lecture Ultrasound of the heart Dr P Wilde, Bristol	CONSENSUS WORKSHOP RADIOLOGY AND THE MANAGEMENT
COFFEE IN MED X RAY				
10.45 - 12.00	THE BREAST Invited Review Lecture Axillary recurrence of breast cancer, a challenge for the radiologist Dr N R Moore, Oxford	RADIOTHERAPY AUDIT Invited Review Lectures Dr A Rodger, Edinburgh Dr C D Shaw, London Dr A Hong, Exeter	GASTROINTESTINAL IMAGING	OF BONE TUMOURS Organiser Dr D Stoker, London
12.15 - 1.15	OXFORD ROOM Presidential Address Professor C A Joslin			
LUNCH IN MED X RAY				
2.30 - 3.45	MUSCULOSKELETAL IMAGING Invited Review Lecture Cross-sectional Imaging of the shoulder joint Professor P Peters, Münster	RADIOTHERAPY FOR PELVIC TUMOURS Invited Review Lecture The place for radiotherapy in the primary management of prostate cancer Dr D Dearnaley, Sutton	RADIATION PROTECTION Invited Review Lecture Implications of the new ICRP recommendations for medical radiology Dr R H Clarke, NRPB	RADIOSURGERY Invited Review Lectures Dr G R ter Haar, Sutton Dr S Bown, London Mr J Wickham, London
TEA IN MED X RAY				

MONDAY 29 APRIL 8.45-9.00

CLARENCE ROOM

Opening of Radiology & Oncology 91 by BIR President, Professor C A F Joslin

MONDAY 29 APRIL 9.00-10.15

CLARENCE ROOM

THE SPINE

Chairman:	Professor B S Worthington, Nottingham
9.00-9.20 *Invited Review*	**Intradiscal therapy for the herniated nucleus pulposus in the lumbar spine** Dr I McCall, Oswestry *(p.1)*
9.20-9.28	**The role of MRI in the assessment of acute and sub-acute cord syndromes** L A Mitchell, Nottingham *(p.1)*
9.28-9.32	**MRI myelogram contrast at 0.5 and 1.5T** T W Redpath, Coventry *(p.2)*
9.32-9.40	**High dose myelography: The neuroradiological experience** S F S Halpin, London *(p.2)*
9.40-9.44	**The appearance of posterior osteophytes on high definition computed tomography before and after sound anterior cervical fusions** A G Clifton, London *(p.2)*
9.44-9.52	**Low back pain in general practice: Do lumbar spine radiographs influence patient management?** R Marsh, Newcastle-upon-Tyne *(p.2)*
9.52-10.00	**Radiographic examination of the lumbar spine in a community hospital: How many are really necessary?** S F S Halpin, London *(p.3)*

BALMORAL ROOM

FRACTIONATION IN PALLIATIVE RADIOTHERAPY

Chairman:	Professor A Horwich
9.00-9.20 *Invited review*	**T'were best t'were done quickly: a guiding Invited Review principle for palliative radiotherapy** Dr T J Priestman, Wolverhampton *(p.5)*
9.20-9.28	**Conservative surgery and radiation therapy in Stages I and II breast carcinoma: Local control and cosmetic outcome** A Roelstraete, Ghent *(p.5)*
9.28-9.36	**Radio-iodine dose response in differentiated thyroid carcinoma** M E A O'Connell, Sutton *(p.5)*
9.36-9.40	**Local recurrence following conservative surgery and radiotherapy in early breast cancer: The experience of a regional radiotherapy centre** A D Stockdale, Guildford *(p.6)*
9.40-9.44	**A simple asymmetric field matching technique for intact breast irradiation** A J Moloney, Nottingham *(p.6)*
9.44-9.48	**Measurement of the mucositic changes in the oral cavity** T Ljubenov, Bulgaria *(p.6)*

LANCASTER ROOM

IMAGING IN ONCOLOGY

Chairman:	Dr I Kenny, Brighton
9.00-9.20 *Invited Review*	**MR of childhood tumours; present application and future perspectives** Dr M Hall-Craggs, London *(p.7)*
9.20-9.28	**Staging of oesophageal carcinoma: MRI compared with CT** D Glew, Bristol *(p.7)*
9.28-9.32	**Computed tomographic appearances following pleuro-pneumonectomy for malignant mesothelioma** H Adams, Cardiff *(p.7)*
9.32-9.40	**CT evaluation of lymph node status in prostate cancer** J A Spencer, Oxford *(p.8)*
9.40-9.48	**Radiological evaluation of ileal loop diversion following cystectomy for bladder cancer** J Noble, London *(p.8)*
9.48-9.52	**Radiological and pathological correlation in renal lymphoma** S A V Holmes, London *(p.8)*
9.52-10.00	**The role of lymphography in comparison to CT scanning in the management of carcinoma of the cervix** I Fernando, London *(p.9)*
10.00-10.08	**MRI and immunoscintigraphy using indium-111- labelled OC125 in the diagnosis of suspected primary and recurrent ovarian carcinoma** R W Kerslake, Nottingham *(p.9)*
10.08-10.16	**MRI findings in recurrent pelvic tumour** J M Hawnaur, Manchester *(p.9)*

NORFOLK ROOM

CONSENSUS WORKSHOP (9.00-12.00): CAN YOUR RADIOLOGY DEPARTMENT BE FINANCIALLY VIABLE IN THE WAKE OF THE GOVERNMENT WHITE PAPER CHANGES?

Organiser & Chairman:	Dr G de Lacey, Middlesex
Panel:	**P Armstrong, London** **R Atkinson, Norwich** **M Brindle, Kings Lynn** **C Connolly, ASLAN Medical Consultants** **S Glouberman, London** **J Hutton, York** **A Porter, Ashford** *(p.4)*

MONDAY 29 APRIL 10.45-12.00

CLARENCE ROOM

IMAGING AND THE CHEST

Chairman: Dr A Dixon, Cambridge

10.45-11.05 *Invited Review* **High resolution CT of the lung: Technical factors and clinical indications**
Dr A G Wilson, London *(p.11)*

11.05-11.13 High resolution CT in pulmonary sarcoidosis: the significance of peribronchial disease
P M Taylor, Manchester *(p.11)*

11.13-11.21 Accuracy of high resolution computed tomography versus chest radiography in chronic diffuse infiltrative lung disease
S Padley, London *(p.11)*

11.21-11.25 Computed tomography of the thorax in chronic berylliosis
K M Harris, South Glamorgan *(p.12)*

11.25-11.33 The role of computed tomography in the early diagnosis of invasive pulmonary aspergillosis
C M Owens, London *(p.12)*

11.33-11.41 An anatomical and functional correlation of disease activity in fibrosing alveolitis: High resolution computed tomography (HRCT) and ^{99}Tc^{m} scanning
D M Hansell, London *(p.12)*

11.41-11.45 The utility of medium-section CT through the subaortic fossa in bronchogenic carcinoma
A Gillams, London *(p.13)*

11.45-11.53 A CT study of the incidence of mediastinal lymphadenopathy in asbestosis
C Sampson, London *(p.13)*

11.53-11.57 Atypical chest radiograph manifestations of pneumocystis pneumonia
K T Tung, London *(p.13)*

11.57-12.05 Q fever acute chest X-ray appearances in 55 cases
R M Wellings, Birmingham *(p.13)*

BALMORAL ROOM

TEACH-IN:
RADIOTHERAPY OF BRAIN TUMOURS

Organiser: Dr R Rampling, Glasgow *(p.15)*

LANCASTER ROOM

DIAGNOSTIC WORK IN PROGRESS SESSION

Chairman: Dr R Corbett, Glasgow

DUKES SUITE

INTERVENTIONAL ANGIOGRAPHY

Chairman: Dr A Adam, London

10.45-10.53 Femoro-distal vein graft angioplasty: A disappointment?
R Uberoi, Bristol *(p.16)*

10.53-11.01 Preliminary clinical experience with intravascular stents in the iliac and femoral vessels
M R Rees, Leeds *(p.16)*

11.01-11.05 The management of intra-renal vascular abnormalities
S A V Holmes, London *(p.16)*

11.05-11-13 High speed rotational angioplasty using the Kensey catheter - early and long term results
J F Dyet, Hull *(p.17)*

11.13-11.17 Hydrophilic guidewires in recanalisation of occluded femoral and popliteal arteries. Results of a prospective randomised control trial
G G Hartnell, Bristol *(p.17)*

11.17-11.25 Predicting the outcome of percutaneous transluminal angioplasty: Plymouth results
R A Morgan, Plymouth *(p.17)*

11.25-11.29 Spontaneous variability of success of peripheral percutaneous angioplasty (PTA) makes the use of historical control groups invalid
A M Jones, Bristol *(p.18)*

11.29-11.33 Thrombolysis in high risk patients
F V Gleeson, London *(p.18)*

11.33-11.41 The use of isotope limb blood flow in the assessment of peripheral angioplasty
P J Thorley, Leeds *(p.18)*

11.41-11.45 A return to vasodilatation for demonstration of distal vessels
K P Gill, London *(p.19)*

11.45-11.53 Evaluation of peripheral angioplasty using intra- arterial Doppler ultrasound
G G Hartnell, Bristol *(p.19)*

11.53-12.01 Clinical application of intravascular ultrasound in arterial disease
P J Scott, Leeds *(p.19)*

MONDAY 29 APRIL 12.15-1.15

OXFORD ROOM

MACKENZIE DAVIDSON MEMORIAL LECTURE

Advances in basic science - have they benefited patients with cancer?
Professor S Dische, Middlesex *(p.20)*

MONDAY 29 APRIL 2.30-3.45

CLARENCE ROOM

RADIOLOGICAL HISTORY

Chairmen: Dr J Guy, Yeovil and Professor I Isherwood, Manchester

2.30-2.50 **The history of angiography**
Invited Review Professor R G Grainger, Sheffield *(p.21)*

2.50-3.10 **Historical experiments predating commer-cially available computed tomography (CT)**
Invited Review Dr S Webb, Sutton *(p.21)*

3.10-3.30 **The origins of radiological apparatus**
Invited Review Dr W D Hackmann, Oxford *(p.21)*

3.30-3.34 **Seeing with sound ... a medical adventure starting during the fifties**
R van Tiggelen, Brussels *(p.22)*

3.34-3.42 **Reception of W C Roentgen's detection of X-rays in German, Austrian newspapers and journals**
H J Maurer, Kuala Lumpur *(p.22)*

3.42-3.50 **Perceptions of radiology in the management of diseases of bones and joints**
J Guy, Somerset *(p.22)*

BALMORAL ROOM

ARE RADIOTHERAPY MACHINES USER FRIENDLY?

Chairman: Mr R Mark, Sussex

2.30-2.50 **A Physicist's View**
Invited Review Mr J B Tuohy, Leeds *(p.23)*

2.50-3.10 **A Radiographer's View**
Invited Review Mrs M Granville-White, Nottingham *(p 23)*

3.10-3.18 **Evaluation of MOSFET detectors as radiation dosimeters for radiotherapy beams**
M Soubra, Ontario *(p.23)*

3.18-3.26 **Optimised three-dimensional treatment planning using a multi-leaf collimator**
S Webb, Sutton *(p.23)*

3.26-3.30 **The advantages of proton beam radiotherapy**
A E Nahum, Sutton *(p.24)*

3.30-3.34 **Evaluation of a radiotherapy electronic portal imaging device**
C Nalder, London *(p.24)*

3.34-3.38 **A rectal applicator for use with a selectron**
R Orpwood, Bath *(p.24)*

3.38-3.42 **One year's experience with the first Therapax Series 3 superficial treatment unit**
H M Morgan, Bath *(p.25)*

LANCASTER ROOM

TEACH-IN:
PLANNING RADIOTHERAPY TREATMENT FOR GYNAECOLOGICAL CANCER

Organiser: Dr R Hunter, Manchester *(p.26)*

NORFOLK ROOM

DOPPLER ULTRASOUND

Chairman: Dr W Hateley, London

2.30-2.50 **The current state of Doppler flow imaging**
Invited Review Professor J Woodcock, Cardiff *(p.27)*

2.50-2.58 **Comparison of colour Doppler ultrasound with venography in central vein thrombosis**
GM Baxter, Glasgow *(p.27)*

2.58-3.06 **Venous ultrasound in the thigh; normal variants and potential pitfalls**
G R J Sissons, Cardiff *(p.27)*

3.06-3.10 **The value of duplex Doppler in detecting hepatic artery thrombosis following liver transplantation**
R M Wellings, Birmingham *(p.28)*

3.10-3.18 **Umbilical artery Doppler ultrasound in the antenatal assessment of the growth discrepant twin pregnancy**
S J Stinchcombe, Nottingham *(p.28)*

3.18-3.22 **Duplex Doppler ultrasound: An easy non-invasive way to detect alterations in renal blood flow during infusion of dopamine**
I Mastorakou, Oxford *(p.28)*

3.22-3.26 **Doppler untrasound of renal artery blood flow following transplantation: How reproducible are the measurements?**
J M Fields, Manchester *(p.29)*

3.26-3.34 **Colour Doppler and cavernosometry in the evaluation of impotence**
S Hampson, London *(p.29)*

3.34-3.38 **Duplex Doppler ultrasound in the investigation of occult nephropathy following the haemolytic uraemic syndrome**
F V Gleeson, London *(p.29)*

3.38-3.46 **Is there a place for colour Doppler ultrasound in the assessment of retrobulbar eye flow?**
G M Baxter, Glasgow *(p.30)*

DUKES SUITE

TECHNIQUES AND TECHNOLOGY IN MAGNETIC RESONANCE

Chairman: Professor M Smith, Leeds

2.30-2.38 **The clinical potential of rapid T1 mapping of the brain using multi-slice IR-Echo-Planar Imaging**
B S Worthington, Nottingham *(p.31)*

2.38-2.46 **Clinical use of anisotropically restricted diffusion in MRI of the nervous system**
G M Bydder, London *(p.31)*

2.46-2.50 **The determination of feature length from magnetic resonance image data**
N Roberts, Liverpool *(p.31)*

2.50-2.58 **A review of parameterisation in MRI for performance evaluation**
J P Bean, London *(p.32)*

2.58-3.02 **Alterations in contrast in magnetic resonance imaging produced by saturation transfer and spin locking techniques**
C J Baudouin, Middlesex *(p.32)*

3.02-3.10 **A rapid and accurate multipoint imaging measurement of T1 relaxation times using the TOMROP sequence**
M O Leach, Sutton *(p.32)*

3.10-3.18 **Further developments of high temperature superconducting receiver coils**
A S Hall, Middlesex *(p.32)*

3.18-3.22 **Localised spectroscopic T1 relaxation time measurements using a two point IR/SR sequence**
N M Yongbi, Sutton *(p.33)*

3.22-3.30 **The role of performance assessment in the selection acceptance and quality assurance of MRI**
J A Lunt, London *(p.33)*

3.30-3.38 **Installation and initial experience of operating a 0.2T permanent magnet MRI system**
R Bodley, Aylesbury *(p.33)*

3.38-3.46 **Some effects of prolonged rf irradiation**
I R Young, Middlesex *(p.34)*

MONDAY 29 APRIL 4.15-5.30

CLARENCE ROOM

TECHNIQUES AND TECHNOLOGY IN DIAGNOSTIC IMAGING

Chairman: Dr A Carty, Liverpool

4.15-4.35 **Experiences with echo-contrast media**
Invited Review Dr P N Burns, Philadelphia *(p.35)*

4.35-4.39 **Radiation pressure gradients and acoustic streaming in ultrasound fields**
H C Starritt, Bath *(p.35)*

4.39-4.47 **Theoretical models for the luminescence of X-ray phosphor screens**
G E Giakoumakis, Greece *(p.36)*

4.47-4.55 **Portable chest radiography on the intensive care unit: A comparison of computed and conventional radiography**
P E Jennings, London *(p.36)*

4.55-4.59 **Colour flow computed tomography**
K A Miles, Cambridge *(p.36)*

4.59-5.07 **3D imaging of soft tissues**
J E Gardener, London *(p.36)*

5.07-5.11 **3D demonstration of biliary anatomy in obstructive jaundice**
A Gillams, London *(p.37)*

5.11-5.19 **Semi-automatic quantitative evaluation of digitized skeletal radiographs**
W Golder, Munich *(p.37)*

5.19-5.27 **Image quality in computed radiology**
A Workman, Leeds *(p.37)*

BALMORAL ROOM

TEACH-IN:
UPDATE ON PAEDIATRIC GASTRIC STUDIES

Organisers: Dr H Carty, Liverpool
Dr D Shaw, London *(p.38)*

LANCASTER ROOM

DIAGNOSTIC WORK IN PROGRESS

Chairman: Dr R Corbett, Glasgow

NORFOLK ROOM

ONCOLOGY WORK IN PROGRESS

Chairman: Dr R G B Evans, Newcastle

TUESDAY 30 APRIL 9.00-10.15

CLARENCE ROOM

BODY MRI

Chairman: Professor I Isherwood, Manchester

9.00-9.20 **MRI of major mediastinal vessels**
Invited Review Professor D Foley, Milwaukee *(p.39)*

9.20-9.24 **The contribution of MRI in the assessment of suspected uterine enlargement**
R W Kerslake, Nottingham *(p.39)*

9.24-9.32 **MR guided biopsy**
H Baddeley, Northwood *(p.39)*

9.32-9.36 **MRI in the problem pelvis**
J Kabala, Bristol *(p.40)*

9.36-9.44 **Pulse sequence selection in the evaluation of ovarian pathology**
B S Worthington, Nottingham *(p.40)*

9.44-9.52 **Clinical applications of magnetic resonance imaging in children**
A R Wright, Newcastle-upon-Tyne *(p.40)*

9.52-9.56 **MRI of cerebellopontine angle lesions - the role of gadolinium-DTPA**
D G Hughes, Manchester *(p.41)*

9.56-10.04 **Congenital uterine anomalies: MRI evaluation**
B M Carrington, Manchester *(p.41)*

10.04-10.08 **Magnetic resonance imaging using the STIR sequence in the preoperative localisation of parathyroid adenomas**
A R Wright, Newcastle-upon-Tyne *(p.41)*

10.08-10.12 **The marrow in sickness and in health; an MRI insight**
S Blease, Bristol *(p.42)*

10.12-10.20 **Assessment of extra occular orbital pathology using magnetic resonance imaging**
P Goddard, Bristol *(p.42)*

BALMORAL ROOM

FRACTIONATION IN RADICAL RADIOTHERAPY

Chairman: Dr W Jones, Leeds

9.00-9.20 **Accelerated fractionation**
Invited Review Professor A Horwich, Sutton *(p.43)*

9.20-9.28 **Continuous, hyperfractionated, accelerated radiotherapy (CHART) at Mount Vernon**
M I Saunders, Northwood *(p.43)*

9.28-9.36 **Parotid gland function following accelerated and conventionally fractionated radiotherapy**
M D Leslie, Northwood *(p.44)*

9.36-9.44 **Accelerated radiotherapy for carcinoma of the breast**
J Krawczyk, Portsmouth *(p.44)*

9.44-9.52 **Carcinoma of the thoracic oesophagus treated by radiotherapy - the Mount Vernon experience 1980 - 1989**
M D Leslie, Northwood *(p.44)*

9.52-10.00 **Combined external beam and high dose rate intracavitary radiotherapy for carcinoma of the nasopharynx - preliminary results**
J B Wang, China *(p.44)*

10.00-10.08 **Magnetic resonance imaging in the diagnosis of radiation myelitis**
H Baddeley, Northwood *(p.45)*

LANCASTER ROOM

THE THERAPEUTIC USES OF NEW ISOTOPES

Chairman: Dr V J Lewington, Southampton

9.00-9.20 **I-131 MIBG therapy in the treatment of**
Invited Review **neuroblastoma**
Dr C A Hoefnagel, Amsterdam *(p.46)*

9.20-9.40 **The principles of radionuclide therapy**
Invited Review Prof. D M Ackery, Southampton *(p.46)*

9.40-10.00 **Prostatic carcinoma: Strontium-89 ther-**
Invited Review **apy for metastatic bone pain**
Dr V J Lewington, Southampton *(p.46)*

10.00-10.20 **Radionuclide therapy for medullary thy-**
Invited Review **roid cancer**
Dr S E M Clarke, London *(p.47)*

NORFOLK ROOM

MANAGEMENT & AUDIT IN RADIOLOGY

Chairman: Dr J P Owen, Newcastle-upon-Tyne

9.00-9.20 **Diagnostic imaging in primary health**
Invited Review **care**
Dr J P Owen, Newcastle-upon-Tyne *(p 48)*

9.20-9.40 **Improving clinical management through**
Invited Review **diagnostic imaging**
Dr I T Russell, Aberdeen *(p.48)*

9.40-9.48 **Clinical audit in radiology departments using a casemix system**
P Hoffman, London *(p.48)*

9.48-9.56 **Audit of out of hours CT scan usage in a city centre hospital**
M J Weston, Bristol *(p.48)*

9.56-10.04 **Audit in action: Significant reduction of barium enema screening time with no loss of examination quality**
D Horton, Hull *(p.49)*

10.04-10.12 **Does the child need an advocate?**
C Gyll, Brighton *(p.49)*

TUESDAY 30 APRIL 10.45-12.00

CLARENCE ROOM

THE LIVER

Chairman: Dr H Nunnerly, London

10.45-11.05 Liver imaging
Invited Review Professor A Baert, Leuven *(p.50)*

11.05-11.25 Intraoperative ultrasound and liver surgery
Invited Review Dr G Plant, Basingstoke *(p.50)*

11.25-11.33 Gastric carcinoma - does intra-operative ultrasound affect the surgical management?
M Bradley, Liverpool *(p.50)*

11.33-11.37 Review of hepatic segmental anatomy
E A O'Grady, Liverpool *(p.51)*

11.37-11.45 Lipiodol CT in patients with malignant liver tumours - is it worth the trouble?
P Dawson, London *(p.51)*

11.45-11.49 The CT central dot sign in bile duct dilatation - a non-specific finding
J S Beswick, Manchester *(p.51)*

11.49-11.57 Dynamic computed tomography in the assessment of liver blood flow in normal and cirrhotic livers
K A Miles, Cambridge *(p.52)*

BALMORAL ROOM

BIOLOGICAL TREATMENT IN ONCOLOGY

Chairman: Dr N J McNally, Northwood

10.45-11.05 Biological therapies in oncology
Invited Review Professor P Selby, Leeds *(p.53)*

11.05-11.13 Labelling index as a predictor of repopulation in human tumours
N J McNally, Northwood *(p.53)*

11.13-11.21 Combined 131 iodine metaiodobenzylguanidine (131mIBG) and high dose chemotherapy (HDT) with bone marrow rescue (ABMT) in poor prognosis neurblastoma
R Corbett, Sutton *(p.53)*

11.21-11.29 Arterial infusion of adriamycin for hepatoma. Can addition of lipiodol allow dose modifications?
N Raby, London *(p.54)*

11.29-11.33 Transcatheter arterial cytotoxic infusion for hepatoma. Is addition of lipiodol beneficial?
N Raby, London *(p.54)*

11.33-11.37 The significance of continuous following of tumour markers CEA, TPA CA 125, and TATI during control of endometrial cancer
Z Stanojević, Yugoslavia *(p.54)*

11.37-11.41 Serum TPA, CA125 and TATI levels in post-operative residual endometrial cancer
N Potić Zečević, Yugoslavia *(p.55)*

11.41-11.45 An effect of radiotherapy on tissue polypeptid antigen (TPA) and tumour associated trypsin inhibitor (TATI) levels on inoperable cervix cancer patients
M Milutinović, Yugoslavia *(p.55)*

11.45-11.49 Early detection of relapse after complete remission following treatment for metastatic germ cell tumour of the testis
I Brand, Leeds *(p.55)*

LANCASTER ROOM

DIAGNOSTIC IMAGING - PROFFERED PRESENTATIONS

Chairman: Dr J P Owen, Newcastle-upon-Tyne

10.45-10.53 The thymus gland in children: Ultrasound is the imaging method of choice
P I Ignotus, London *(p.56)*

10.53-10.57 A comparison of abdominopelvic computed tomography with ultrasound
W J Shatwell, Oxford *(p.56)*

10.57-11.01 Influence of experience on phlebographic diagnosis of deep venous thrombosis
T Y K Chan, London *(p.56)*

11.01-11.09 Light reflective rheography as a first line imaging method for lower limb deep venous thrombosis
I Harris, Liverpool *(p.57)*

11.09-11.13 Silent deep venous thrombosis and unreliability of clinical diagnosis
T Y K Chan, London *(p.57)*

11.13-11.21 Overlapping biliary endoprostheses - how to solve the problem of stent occlusion
A Adam, London *(p.57)*

11.21-11.25 Direct puncture venography (cavernography) in the assessment of subcutaneous cavernous haemangiomata
A H Troughton, Plymouth *(p.58)*

11.25-11.33 Ultrasound and ultrasound guided fine needle aspiration in cervical lymphadenopathy
R M Evans, Hong Kong *(p.58)*

11.33-11.37 Radiological differential diagnosis between developmental anomalies and bony destruction of the foramen ovale and the foramen spinosum in patients with nasopharyngeal carcinoma
J B Wang, China *(p.58)*

11.37-11.41 **X-linked deafness, stapes gushers and a distinctive defect of the inner ear**
P D Phelps, London *(p.58)*

11.41-11.49 **The role of computed tomography in planning endoscopic paranasal sinus surgery**
M J Warren, Oxford *(p.59)*

11.49-11.53 **Osteoporosis and chemotherapy induced early menopause**
M A Ratcliffe, Aberdeen *(p.59)*

11.53-12.01 **Contrast media reactions in patients with HIV disease**
A K Banerjee, London *(p.59)*

NORFOLK ROOM

CENTRAL NERVOUS SYSTEM

Chairman: Professor B S Worthington, Nottingham

10.45-11.05 *Invited Review* **A critical approach to selecting patients for MRI of the nervous system**
Dr I Moseley, London *(p.61)*

11.05-11.13 **Temporal lobe epilepsy: MRI appearancesand pathological findings**
C S Barker, Oxford *(p.61)*

11.13-11.17 **An audit of MRI in the diagnosis of multiple sclerosis**
N Akhtar, Truro *(p.61)*

11.17-11.25 **Does cranial MR support the statistical link between sinusitis and multiple sclerosis?**
S Blease, Bristol *(p.62)*

11.25-11.33 **A longitudinal MR imaging study of neurological manifestations of HIV infection in a cohort of HIV positive haemophiliac children**
P H B Bolton-Maggs, Liverpool *(p.62)*

11.33-11.37 **Can we reduce eye lens dose during brain CT in the UK?**
L J Yeoman, London *(p.62)*

11.37-11.45 **Magnetic resonance imaging of normal white matter myelination patterns**
A G Clifton, London *(p.63)*

11.45-11.49 **Subjective CT appearance of increased attenuation of an intracerebral artery does not always represent thrombosis**
B C M Macpherson, Glasgow *(p.63)*

11.49-11.57 **Computerised tomography of the brain in the elderly - Too much, too late?**
M S Bernard, Cardiff *(p.63)*

11.57-12.01 **Intracranial osteochondromas: Diagnosis by CT with 3D image reconstruction**
P Grech, London *(p.64)*

TUESDAY 30 APRIL 12.15-1.15

OXFORD ROOM

3M MAYNEORD MEMORIAL LECTURE

Professor D M Goldenberg, New Jersey
New advances in cancer imaging and therapy with radiolabelled antibodies *(p.65)*
(Supported by 3M UK plc)

TUESDAY 30 APRIL 2.30-3.45

CLARENCE ROOM

IMAGING IN TRAUMA

Chairman: Dr A M Davies, Birmingham

2.30-2.50 *Invited Review* **Radiological Services at the Queen's Medical Centre, Nottingham, for the M1 air crash**
Dr B Preston, Nottingham *(p.66)*

2.50-2.58 **Preparing a radiology department major accident plan**
D I Boxer, London *(p.66)*

2.58-3.02 **A new CT method for demonstrating the site of CSF leakage**
M N H Lloyd, Southampton *(p.66)*

3.02-3.10 **An audit of computed tomography in blunt abdominal trauma**
A R Padhani, Cambridge *(p.66)*

3.10-3.18 **The lateral neck radiograph for suspected impacted fish bones - is it indicated?**
R M Evans, Hong Kong *(p.67)*

3.18-3.22 **3-dimensional imaging of tibial plateau fractures**
J N P Higgins, London *(p.67)*

3.22-3.30 **The assessment of groin pain in athletes by peritoneography with CT**
S Blease, Swindon *(p.67)*

3.30-3.38 **MRI in the pre-operative assessment of urethral trauma**
B M Carrington, Manchester *(p.68)*

BALMORAL ROOM

LOW OR HIGH DOSE RATE IN BRACHYTHERAPY?

Chairman: Dr G P Deutsch, Brighton

2.30-2.50 *Invited Review* **Low or high dose rate in brachytherapy? The clinician's choice**
Dr R Stout, Manchester *(p.69)*

2.50-3.10 *Invited Review* **Low or high dose rate in brachytherapy?**
Dr I Turesson, Gothenburg *(p.69)*

3.10-3.18 **Changing an LDR - into an HDR-brachytherapy: How many equivalent factors are necessary?**
R Schulz-Wendtland, Freiburg *(p.69)*

3.18-3.26 **Comparison of intracavitary insertions using iso- effect surfaces**
C Deehan, Glasgow *(p.70)*

LANCASTER ROOM

TEACH-IN: RADIOLOGY IN THE MANAGEMENT OF LYMPHOMA

Organiser &
Chairman: Dr S J Golding, Oxford
Panel: A Jones, Oxford
C Bunch, Oxford
D Brown, Oxford *(p.71)*

NORFOLK ROOM

NUCLEAR MEDICINE - GENERAL SESSION

Chairmen: Dr R Burwood, Brighton and
Professor P J Ell, London

2.30-2.50 **New instrumentation in clinical nuclear medicine**
Invited Review
Professor P J Ell, London *(p.72)*

2.50-2.58 **Computer assisted interpretation of SPECT scans of the brain: A multi-modal approach**
E D Lehmann, London *(p.72)*

2.58-3.06 **Cranial computed tomography and SPET in Alzheimer's Disease**
C S Barker, Oxford *(p.72)*

3.06-3.10 **Evaluation of 11C-methionine uptake in breast cancer metastases using positron emission tomography (PRT)**
R Huovinen, Finland *(p.73)*

3.10-3.18 **A comparison of DMSA and MCU in the investigation of children with proven urinary tract infection**
F V Gleeson, London *(p.73)*

3.18-3.22 **Metastatic squamous carcinoma in the neck: An anatomical and physiological study using CT and SPECT ^{99}Tc^{m} (V) DMSA**
J C Watkinson, London *(p.73)*

3.22-3.26 **Value of MRI in recurrent medullary cell carcinoma of the thyroid: Comparison with pentavalent ^{99}Tc^{m} DMSA scintigraphy**
R Chaudhuri, London *(p.74)*

3.26-3.34 **^{67}Gallium citrate scintigraphy in the investigation of human immunodeficiency virus positive patients with pyrexia of undetermined origin**
J R Buscombe, London *(p.74)*

3.34-3.38 **Arterial oxygen saturation during isotope perfusion scans using macroaggregates of albumin**
S A Renowden, Cardiff *(p.74)*

3.38-3.42 **An audit of non-diagnostic bone scans**
S A Worthy, Liverpool *(p.74)*

3.42-3.46 **^{99}Tc^{m} radio-pharmaceuticals for the X-ray fluorescence assessment of gold in vivo**
J Shakeshaft, Bath *(p.75)*

TUESDAY 30 APRIL 4.15-5.30

OXFORD ROOM

SILVANUS THOMPSON MEMORIAL LECTURE

Dr R J Berry, British Nuclear Fuels plc, Cumbria
Striking a balance: benefit and risk in Man's exposure to manmade radiation *(p.76)*

WEDNESDAY 1 MAY 8.15 - 9.00

CLARENCE ROOM

BIR ANNUAL GENERAL MEETING

(Open to BIR members only)

WEDNESDAY 1 MAY 9.00-10.15

CLARENCE ROOM

URORADIOLOGY

Chairman: Dr S J Golding, Oxford

9.00-9.20 **Magnetic resonance imaging and spectroscopy of the normal and transplant kidney**
Invited Review
Dr A Dixon, Cambridge *(p.77)*

9.20-9.24 **Detection of nonpalpable testes by MRI**
C Kaniklides, Sweden *(p.77)*

9.24-9.28 **Percutaneous nephrostomy (PCN) in the management of upper urinary tract obstruction**
T R Terry, Leicester *(p.77)*

9.28-9.36 **Follow-up of adults with haematuria and negative urography and ultrasound**
T M M Meagher, Oxford *(p.78)*

9.36-9.40 **Is bowel preparation necessary before intravenous urography?**
C D George, London *(p.78)*

9.40-9.48 **The antenatally diagnosed multicystic kidney and the role of postnatal imaging**
F V Gleeson, London *(p.78)*

9.48-9.52 **Investigation of voiding function and dysfunction following enterocystoplasty**
J Noble, London *(p.78)*

9.52-10.00 **Computed tomography in primary aldosteronism**
P Sanville, Manchester *(p.79)*

10.00-10.04 **Congenital urethral hypoplasia**
F V Gleeson, London *(p.79)*

10.04-10.08 **Anomalous penile venous drainage in erectile dysfunction**
P D Miller, London *(p.79)*

10.08-10.16 **The radiology of urethral stents**
D Rickards, London *(p.80)*

BALMORAL ROOM

QUALITY ASSURANCE IN RADIOTHERAPY

Chairman: Professor N Bleehan, Cambridge

9.00-9.20 **Quality assurance in radiotherapy (QUART)**
Invited Review
Mrs S Williams, Newcastle-upon-Tyne *(p.81)*

9.20-9.40 **Quality assurance in radiotherapy: Clinical aspects**
Invited Review
Dr R G B Evans, Newcastle *(p.81)*

9.40-10.00 **Quality assurance in radiotherapy: Physical aspects**
Invited Review
Dr P C Williams, Manchester *(p.81)*

10.00-10.04 **Quality assurance in radiation therapy**
P deSilva, Ontario *(p.82)*

10.04-10.08 **Initial experience of megavoltage imaging for breast treatment verification**
M C Kirby, Manchester *(p.82)*

10.08-10.12 **Use of pre-defined shapes for producing irregular fields with a multileaf collimator**
P C Williams, Manchester *(p.82)*

10.12-10.16 **Performance characteristics of the Philips multileaf collimator**
P C Williams, Manchester *(p.83)*

LANCASTER ROOM

CONSENSUS WORKSHOP (9.00-12.00): THE MANAGEMENT OF BONE TUMOURS

Organiser & Chairman: Dr D J Stoker, London
Panel: Professor R L Souhami, London
Dr J Pringle, London
Mr S R Cannon, London *(p.84)*

NORFOLK ROOM

CARDIOVASCULAR IMAGING

Chairman: Professor G Whitehouse, Liverpool

9.00-9.20 **Ultrasound of the heart**
Invited Review
Dr P Wilde, Bristol *(p.85)*

9.20-9.28 **Transeptal ballon mitral valvoplasty: Initial results using the Inoue technique**
E F Brown, Bristol *(p.85)*

9.28-9.32 **Diseases of the thoracic aorta: Comparison of MRI with transesophageal echocardiography and angiography for diagnosis**
R MacMillan, Philadelphia *(p.85)*

9.32-9.40 **Application of magnetic resonance velocity mapping to measurement of flow through healthy and stenotic mitral valves**
R H Mohiaddin, London *(p.86)*

9.40-9.44 **Pulmonary scintigraphy in pulmonary embolism: How often does it change clinical management?**
P G White, Cardiff *(p.86)*

9.44-9.48 **MRI and coarctatiion of the aorta: Imaging structure and function**
R A Coulden, Manchester *(p.86)*

9.48-9.56 **Quantitative MR-angiography of patients with pulmonary hypertension**
E Dinkel, Freiburg *(p.87)*

9.56-10.00 **Topography of deep venous thrombosis**
T Y K Chan, London *(p.87)*

10.00-10.04 **Abdominal aortic aneurysm - problems in CT assessment of renal artery involvement**
C E Williams, Liverpool *(p.87)*

10.04-10.08 **Use of colour 3-dimensional imaging in abdominal arterial aneurysm**
J N P Higgins, London *(p.88)*

10.08-10.16 **Measurement of regional left ventricular function using labelled magnetic resonance imaging**
M B Buchalter, Cambridge *(p.88)*

WEDNESDAY MAY 1 10.45-12.00

CLARENCE ROOM

THE BREAST

Chairman: Professor G Whitehouse, Liverpool

10.45-11.05 *Invited Review* **Axillary recurrence of breast cancer, a challenge for the radiologist**
Dr N R Moore, Oxford *(p.89)*

11.05-11.13 **Digital image processing of X-ray and MR breast images**
S L Free, London *(p.89)*

11.13-11.17 **The assessment of screen detected mammographic abnormalities. When is the decision to operate made?**
G R Cherryman, Nottingham *(p.89)*

11.17-11.25 **A test object for evaluating the image quality of photo-stimulable phosphor computed mammography**
D S Brettle, Leeds *(p.90)*

11.25-11.29 **The combined effects of breast composition and size in determining radiation risks from mammography**
A P Hufton, Manchester *(p.90)*

11.29-11.37 **The predictive value of mammographic abnormalities as assessed in a screening programme**
G R Cherryman, Nottingham *(p.90)*

11.37-11.41 **Small lesions in mammography: Stereotactical localisation for cytological puncture and histological biopsy**
M Bauer, Freiburg *(p.91)*

11.41-11.45 **Predicting outcome in mammography: Parenchymal patterns and other approaches**
A G Gale, Nottingham *(p.91)*

11.45-11.53 **Audit in action: Mammography in women under 35 with symptomatic breast disease**
I R Brand, Bradford *(p.91)*

11.53-11.57 **In vivo localised ^{31}P spectroscopy of human breast carcinoma**
J Glaholm, Sutton *(p.91)*

11.57-12.05 **Mammographic film interpretation**
A G Gale, Nottingham *(p.92)*

BALMORAL ROOM

RADIOTHERAPY AUDIT

Chairman: Dr C Paine, Oxford

10.45-11.05 **Have we, can we, should we?**
Invited Review Dr A Rodger, Edinburgh *(p.93)*

11.05-11.25 **We must**
Invited Review Dr C D Shaw, London *(p.93)*

11.25-11.45 **What we have done**
Invited Review Dr A Hong, Exeter *(p.93)*

NORFOLK ROOM

GASTROINTESTINAL IMAGING

Chairman: Dr T Doyle, Brighton

10.45-10.53 **TC99^{m} HMPAO labelled white cells in acute colitis - a comparison with plain films and air insufflation**
J Hughes, Cardiff *(p.94)*

10.53-10.57 **Barium meal diagnosis of Coeliac disease**
S J Armstrong, Bristol *(p.94)*

10.57-11.05 **Abdominal ultrasound as the primary diagnostic procedure in patients with suspected small bowel Crohn's disease**
D A Nicholson, Manchester *(p.94)*

11.05-11.09 **Defaecating videoproctography following restorative proctocolectomy**
M M J McNicholas, Dublin *(p.94)*

11.09-11.13 **Balloon dilatation of anastomotic rectal strictures**
K D McBride, Dublin *(p.95)*

11.13-11.21 **Gastrointestinal lumenal cytology: a radiological procedure**
S J Morris, Bristol *(p.95)*

11.21-11.25 **The role of angiography in the assessment of patients with acute or chronic gastro-intestinal haemorrhage**
S C Whitaker, Nottingham *(p.95)*

11.25-11.29 **The final outcome in GI haemorrhage following normal mesenteric angiography**
D Kinsella, Bristol *(p.96)*

11.29-11.37 **Detection of unsuspected lesions other than gall bladder pathology during cholecystosonography**
B Banerjee, Ashton-under-Lyne *(p.96)*

11.37-11.41 **Herniation of the large bowel through the diaphragmatic oesophageal hiatus**
J Virjee, Bristol *(p.96)*

11.41-11.49 **Prompt radiological diagnosis of retroperitoneal perforation following therapeutic ERCP is important in determining outcome of treatment**
D F Martin, Manchester *(p.96)*

11.49-11.57 **The value of ultrasound examination in patients undergoing ERCP for suspected biliary and pancreatic disease**
J M E Kirk, London *(p.97)*

WEDNESDAY 1 MAY 12.15-1.15

OXFORD ROOM

PRESIDENTIAL ADDRESS

The future and the Institute

Professor C A Joslin

WEDNESDAY 1 MAY 2.30-3.45

CLARENCE ROOM

MUSCULOSKELETAL IMAGING

Chairman: Dr D Stoker, London

2.30-2.50 **Cross-sectional imaging of the shoulder joint**
Invited Review Professor P E Peters, Munster *(p.98)*

2.50-2.58 **Follow-up MRI examinations in rheumatoid arthritis**
A Mundinger, Freiburg *(p.98)*

2.58-3.02 **Notts disease: An atypical erosive arthritis of the hands**
M J Cobby, Michigan *(p.98)*

3.02-3.10 **Angiographic changes in the neuropathic foot**
B Menanteau, Reims *(p.99)*

3.10-3.14 **Does the metacarpal index have a place in making the diagnosis of Marfans Syndrome?**
K A Younger, London *(p.99)*

3.14-3.22 **MR imaging in dialysis related amyloid arthropathy**
M J Cobby, Bristol *(p.99)*

3.22-3.26 **Evaluation of osseous lesions of the lower limb by magnetic resonance imaging (MRI)**
J M Hawnaur, Manchester *(p.100)*

3.26-3.34 **Bone cortical and periosteal changes as seen on MRI**
G B Greenfield, Florida *(p.100)*

3.34-3.42 **The incidence and significance of fluid/fluid levels on CT of osseous lesions**
A M Davies, Birmingham *(p.100)*

3.42-3.46 **Magnetic resonance imaging of desmoid tumours**
J Kabala, Bristol *(p.101)*

BALMORAL ROOM

RADIOTHERAPY FOR PELVIC TUMOURS

Chairman: Dr G Rees, Bristol

2.30-2.50 **The place for radiotherapy in the primary management of prostate cancer**
Invited Review Dr D Dearnaley, Sutton *(p.102)*

2.50-2.58 **Computerised image analysis in prostatic neoplasia**
P D Miller, London *(p.102)*

2.58-3.06 **Total cystectomy and substitution enterocystoplasty - an alternative primary treatment for stage T2/3 bladder carcinoma**
S A V Holmes, London *(p.102)*

3.06-3.14 **The post-irradiation bladder: A functional model**
J A Vale, London *(p.103)*

3.14-3.18 **Prostate specific antigen (PSA) in monitoring prostatic carcinoma**
P D Miller, London *(p.103)*

3.18-3.22 **Radical prostatectomy - the treatment of choice for stage T1/2 carcinoma of the prostate?**
T J Christmas, London *(p.103)*

3.22-3.26 **Growth control in prostatic neoplasia**
P D Miller, London *(p.103)*

3.26-3.30 **Maximising local control by customized dose prscription for pelvic tumours**
A E Nahum, Sutton *(p.104)*

3.30-3.34 **Reduction in adverse radiation effect by a simple conformational technique in radiotherapy for early carcinoma of the prostate**
G Read, Manchester *(p.104)*

3.34-3.38 **The management of ureteric stricture following external beam radiotherapy and Wertheim's hysterectomy for cervical carcinoma**
T J Christmas, London *(p.104)*

LANCASTER ROOM

RADIOSURGERY

Chairman: Professor C Hill, Sutton

2.30-2.50 **Ultrasound surgery - a review**
Invited Review Dr G R ter Haar, Sutton *(p.105)*

2.50-2.54 **Ultrasound image enhancement for lithotripsy**
N P Cohen, London *(p.105)*

2.54-3.02 **Initial experiences in the treatment of gallstones by extra corporeal shock wave lithotripsy**
E B Rolfe, Birmingham *(p.105)*

3.02-3.22 **The future of lasers in cancer therapy**
Invited Review Dr S Bown, London *(p.106)*

3.22-3.42 **Minimally invasive surgery**
Invited Review Mr J Wickham, Sutton *(p.106)*

pattern. We conclude that increased lung epithelial permeability in fibrosing alveolitis reflects the extent of lung involvement rather than HRCT appearances alone. Reasons for this apparent discordance are discussed.

The utility of medium-section computed tomography through the subaortic fossa in bronchogenic carcinoma

A. Gillams, D. Hansell, *E. Griffiths and *P. Goldstraw

*Departments of Radiology and *Surgery, The Royal Brompton and National Heart Hospital, London, UK*

In the pre-operative staging of bronchogenic carcinoma, computed tomography (CT) is used to assess the presence and size of mediastinal nodes. For all mediastinal areas, CT has a sensitivity of 79–89% and a specificity of 65–96% in detecting metastases (normal nodes, less than 1 cm). However, partial volume effect from the adjacent vasculature makes the subaortic fossa (SAF) particularly difficult to assess when using a standard 10/10 mm protocol. Our aim was to establish whether medium-section CT through the SAF would improve nodal assessment. Six patients (mean age 64 years, three male and three female) with suspected bronchogenic carcinoma were studied. At surgery the SAF was cleared of all nodes which allowed precise site and size correlation with CT findings. During preoperative staging standard CT (contiguous 10 mm cuts with 100 ml dynamic injection of intravenous contrast) was followed by 6 mm slices at 5 mm intervals through the SAF with a 50 ml bolus of contrast. The two sets of scans were interpreted separately and then compared with the surgical and histological findings. In four cases there was a difference in nodal assessment and in each case the 6 mm slices gave a more accurate depiction of both the size and number. In one of these patients the staging was upgraded on the 6 mm cuts. We conclude that the accurate assessment of this inaccessible region of the mediastinum is significantly improved by the use of medium-section CT.

A computed tomography study of the incidence of mediastinal lymphadenopathy in asbestosis

C. Sampson and D. M. Hansell

Department of Diagnostic Radiology, Royal Brompton and National Heart Hospital, London SW3 6HP, UK

Recent studies have reported a high incidence of significant mediastinal lymphadenopathy in cryptogenic fibrosing alveolitis. This study determined the incidence of mediastinal lymphadenopathy in two groups of asbestos exposed patients, one group with established pulmonary fibrosis and a control group with pleural disease only. The computed tomography scans of male patients who had attended during a 1 year period for investigation following asbestos exposure were reviewed initially on lung windows. A group of 14 patients with calcified pleural plaques and definite pulmonary fibrosis (mean age 70 years) and a control group of 11 patients of similar ages (mean age 67 years) who had calcified plaques confirming asbestos exposure but no parenchymal disease were selected. Cases of malignancy or infection were excluded. Computed tomography sections were imaged on mediastinal windows and the site, size and number of nodes greater than 1 cm in the long axis were recorded. In the pulmonary fibrosis group all cases had at least one enlarged node and the average number of nodes greater then 1 cm was four (range 1–10). In the control group only two cases had one node greater than 1 cm. We conclude that mediastinal lymphadenopathy occurs frequently in asbestosis. Awareness of this is important in the investigation of malignant disease in patients with asbestosis.

Atypical chest radiograph manifestations of pneumocystis pneumonia

K. T. Tung and R. J. Davies

Department of Diagnostic Radiology, Westminster Hospital. Dean Ryle Street, London SW1, UK

A number of unusual manifestations of pneumocystis pneumonia (PCP) have been described including focal or segmental consolidations, nodules, septal lines and apical air cyst formation. Two further radiological patterns on chest radiographs encountered in our practice are presented which, to our knowledge, have not previously been described in the literature. All cases were proven with positive sputum or bronchial washings or by transbronchial biopsy. The first type is a pattern of gross diffuse air cyst formation throughout both lungs. This is a rare manifestation associated with multiple previous treated episodes of PCP. It is also associated with pneumothorax and the prognosis is poor. The second pattern is seen in patients who have been treated with inhaled pentamidine and presents with striking bilateral symmetrical consolidation of the extreme apices without involvement of the remainder of the lungs. It is postulated that this is due to differential distribution of inhaled pentamidine in the lung.

Q fever acute chest radiograph appearances in 55 cases

R. M. Wellings, *D. L. Smith, C. Walker, J. G. Ayers and *P. S. Burge

*Departments of Radiology and *Respiratory Medicine, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST, UK*

We reviewed chest radiographs taken within 20 days of symptom onset in 55 cases of Q fever, diagnosed by standard serology. Thirty lateral films were used to assist in localization of shadowing. All cases were from the large Q fever outbreak in the West Midlands in 1989. Films were viewed and scored separately by two observers. There was agreement in 88.2%. Where opinions differed, the films were jointly reviewed and a consensus agreed. The mean interval (SD) between date of onset of symptoms and date of film was 5.9 (4.3) days (range 0–20). There were six normal films. Shadowing was unilateral in 45 (92%) films and bilateral in four (8%). In the majority of films, shadowing was peripheral (49%); segmental shadowing was seen in 29%, perihilar shadowing in 17% and lobar shadowing in 5%. The nature of the shadowing was homogenous in 72%, rounded in 7.4% and reticular in 6.5%. Linear atelectasis was seen in 2.8%. There was no cavitation. A single zone of six was affected in 31 (63%) films, two zones in 16 (33%) and three zones in two (4%). The shadowing was uniformly ill defined. Left-sided shadowing was more common than right (ratio 3:2). Lower zone shadowing was commonest, middle zone next and upper zone least common (ratio 5:3:2). Air bronchograms were present in 18 (37%) films and a small pleural effusion was seen on one film. We conclude that the appearances of acute chest radiographs in Q fever are varied. Shadowing has a predilection for the lower zones, occurs more commonly on the left, is ill defined, largely homogenous and tends to be peripheral. Appearances may be normal in the first 20 days of illness.

Notes

10.45 – 12.00

Teach-in: Radiotherapy of Brain Tumours

Balmoral Room

Overcoming problems in the radiotherapy of brain tumours

R. Rampling, D.H. Hadley and S. McNee
Beatson Oncology Centre, Western Infirmary, Glasgow G11 6NT, UK

Overall, intrinsic brain tumours carry a poor prognosis. Treatment with radiation has been shown unequivocally to improve survival and there is some evidence of a dose–response relationship. Local failure, however, remains the rule. Prognostic factors may identify a group of patients who are likely to survive longer after radiation treatment, though functional outcome may be compromised. For these patients, it is important to minimize treatment-related morbidity. However, identifying the tumour, defining a treatment volume and achieving a homogenous distribution, remains difficult. The problems of distinguishing tumour from uninvolved brain, particularly in the presence of oedema and surgical change, using CT and MRI data, are explored, especially in relationship to contrast enhancement. The use of direct MRI planning and the treatment of brain tumours are discussed. Conventional radiotherapy planning techniques will be covered including positioning, immobilization, CT and MRI scanning techniques, simulation, target volume delineation, beam configuration and treatment delivery. If the tumour volume can be sufficiently localized, it may be possible to use alternative treatment methods, such as stereotactic or conformational therapy to spare neighbouring normal brain. This would open the way for novel fractionation schemes and dose escalations. These possibilities are discussed.

10.45 – 12.00

Interventional Angiography

Dukes Suite

Femoro-distal vein graft angioplasty: a disappointment?

R. Uberoi, *M. G. Wyatt, *M. Horrocks and G. G. Hartnell
*Departments of Radiodiagnosis and *Vascular Surgery, Bristol Royal Infirmary, Bristol BS2 8HW, UK*

Thirty per cent of femoro-distal grafts fail within one year of operation. This is usually due to graft or run-off stenoses. Repair of these stenoses prior to failure can improve graft patency rates. In 180 consecutive vein grafts performed for claudication or critical ischaemia, 48 occluded of which 19 were successfully salvaged. Twenty-three percutaneous angioplasties (PTA) were performed in 20 patients before graft failure, 12 for graft stenoses (group I) and 11 for run-off stenoses (group II). In group I, five (42%) PTA were initially successful, but one later required surgery. Two restenoses occurred, at 18 months and 23 months. One graft failed following balloon rupture and four repeat PTA were required, two of which were successful. In group II, seven (65%) PTA were initially successful and three repeat PTA were performed. One failed resulting in graft occlusion. Three failures in each group were due to inability to pass a balloon to the lesion. This study confirms that graft patency is difficult to restore following failure. The results of PTA for graft stenoses are poor and surgical intervention is often required. Better results are obtained from PTA of run-off stenoses provided the diseased segment is accessible to dilation.

Preliminary clinical experience with intravascular stents in the iliac and femoral vessels

M. R. Rees, P. Scott, A. R. Essop and P. J. Thorley
Departments of Radiology and Cardiology, Killingbeck Hospital, Leeds LS14 6UQ, UK

Over a period of 6 months, 12 intravenous stents have been implanted. Most of these stents were placed acutely during angioplasty following vessel/limb threatening dissection. Five femoral stents were placed in five patients (Strecker stent Meditech). Seven iliac stents were placed in four patients (six Palmaz stents, one Schneider stent). Five of the iliac stents were placed in conjunction with intravascular ultrasound which was also used in follow-up of these patients. Intravascular ultrasound was invaluable in determining the exact size of stent to use as well as determining if it had been properly placed. No direct complications resulted from the placement of the stents. At follow-up all the iliac stents are patent, intravascular ultrasound demonstrated re-endothelialization of an iliac stent at 2 months. Of the five femoral stents, three are definitely patent with the other two stents to be evaluated. All five of these patients have sustained improvement in symptoms. We conclude that the intravascular stent is an invaluable therapy in acute vessel threatening dissection at angioplasty and in short term follow-up does not appear to cause significant complications.

The management of intra-renal vascular abnormalities

S. A. V. Holmes, T J. Christmas, J. A. Vale, J. E. Dacie and W. F. Hendry
Departments of Urology and Radiology, St Bartholomew's Hospital, London EC1A 7BE, UK

Vascular abnormalities within the kidney, though uncommon, embrace a number of conditions. These include benign vascular tumours such as angioma and angiomyolipoma, and arteriovenous fistulae (AVF) from congenital or acquired causes. Many of these lesions, from whatever primary cause, develop arteriovenous connections which may precipitate their presentation. This is most commonly persistent haematuria but if the AVF are of sufficient volume, cardiovascular symptoms such as hypertension and congestive cardiac failure (CCF) may predominate. In the past, clinically significant AVF were managed by nephrectomy, and then by renal-sparing procedures such as partial nephrectomy, ligation of arteries supplying a fistula or direct vascular repair. The more widespread use of renal angiography and embolization techniques has allowed an earlier, more aggressive renal sparing treatment. We present seven symptomatic cases of intrarenal vascular abnormalities due to angioma and acquired AVF and review their management. Angiography followed by embolization was adopted and successful in five out of seven patients with benign lesions and AVF without significant haemodynamic symptoms. Partial nephrectomy was required for a lesion of uncertain aetiology, and nephrectomy for a large AVF which presented with CCF, and was found to be due to a renal carcinoma. In summary, the value of angiography and embolization techniques are emphasized, providing malignant lesions can be excluded.

High speed rotational angioplasty using the Kensey catheter: early and long term results

J. F. Dyet
Cardiovascular Radiology Unit, Hull Royal Infirmary, Hull HU3 2JZ, UK

The Kensey catheter consists of an 8 French coaxial catheter with a blunt rotating cam at its tip. By means of an electric motor the cam is rotated at up to 80 000 rpm. The system is lubricated by a solution of dextran which contains contrast, thus allowing visualization of the artery during the procedure. It is claimed that the catheter will pulverize non visco-elastic tissue (atheroma) selectively and that the high speed jet of lubricating fluid at right angles to the catheter keeps it centrally within the vessel. The catheter was used to attempt recanalization of occluded arteries in 20 patients. The sites of the lesions were one iliac, 10 superficial femoral arteries, four femoropopliteal segments and five popliteals. The occlusions were in the range 5–25 cm in length (mean 11.5 cm). The recanalization was successful in 17 patients (85%) and there were no early re-occlusions. All patients are having 1 year follow-up angiograms, to be completed by April 1991. Results to date indicate a 1 year success rate of the order of 50%. It is suggested that the Kensey catheter may be useful for recanalizing difficult and chronic occlusions but its ling term success rates are no better than conventional angioplasty.

Hydrophilic guidewires in recanalization of occluded femoral and popliteal arteries: results of a prospective randomized control trial

G. G. Hartnell, A. Jones, R. Parry, *R. N. Baird and K. P. Murphy
*Departments of Radiodiagnosis and *Vascular Surgery, Bristol Royal Infirmary, Bristol BS2 8HW, UK*

Experience suggests that hydrophilic guidewires (glidewire, Terumo Corporation) are one of the most effective methods for crossing occluded arteries. We report a prospective randomized trial of the glidewire in recanalizing occluded femoropopliteal arteries. Thirty-three patients were randomized to have recanalization initially attempted with conventional wires (16 patients) or glidewire (17 patients). In the glidewire group, the recanalization rate was 93% with conventional wires required in 33%. Mean lesion length was 8.9 mm. Mean screening time per procedure was 23.9 minutes (21.2 minutes in successful cases) with a mean of 1.9 wires used per patient, and mean 154 ml contrast. In the control group the recanalization rate was 100% but with glidewire required in 44%. Mean lesion length was 6.4 cm, mean screening time 12.2 minutes with a mean of 1.6 wires per patient, and mean 136 ml contrast. The overall successful recanalization rate was 97%. Although use of glidewires is associated with a very high success rate for femoropopliteal recanalization, it may not be necessary to use it as the initial guidewire. Use of the glidewire to augment conventional guidewire recanalization is frequently required and leads to a very high initial success rate which sets a standard for alternative methods.

Predicting the outcome of percutaneous transluminal angioplasty: Plymouth results

R. A. Morgan and I. P. Wells
Department of Radiology, Derriford Hospital, Plymouth PL6 8DH, UK

The results of percutaneous transluminal angioplasty (PTA) undertaken in centres of excellence have been well documented. Percutaneous transluminal angioplasty is now commonly performed in most District General Hospital radiology departments. The data from 300 cases of PTA performed over a 10 year period were reviewed. Patients were followed up with invasive studies, and in a number of cases angiography. The initial (technical) failure rate for all procedures was 14%. The late failure rate was 34%. The factors predicting technical and late failure were occlusion, poor run-off and age over 70 years. In particular, age over 80 had high predictive value for failure, both early and late (71%). These results are compared with those from other large studies and the implications of age on the success of PTA are discussed.

Spontaneous variability of success of peripheral percutaneous angioplasty makes the use of historical control groups invalid

A. M. Jones, K. P. Murphy and G. G. Hartnell
Department of Radiodiagnosis, Bristol Royal Infirmary, Bristol BS2 8HW, UK

The performance of devices for arterial recanalization is usually measured against historical control groups. This comparison is invalid if there are significant spontaneous variations in success rates for percutaneous angioplasty (PTA) over time. Over 20 months, 316 patients underwent balloon PTA for peripheral vascular disease (120 iliac stenoses, 88 femoropopliteal occlusion, 77 femoropopliteal stenosis, 31 others). Primary success rates for variable period lengths during this study were as follows. The only factor related to primary success rate was the introduction of the glidewire half way through the study period. There was no relationship between success and the proportion of trainees doing PTA, learning curve or proportion of occluded arteries. Percutaneous angioplasty primary success rates are subject to unpredictable variations, over short periods, of up to 16%, making comparison with historical control groups when assessing new devices invalid. There is no substitute for prospective randomized studies with contemporary control groups.

	Overall (%)	Iliac stenosis (%)	Femoropopliteal stenosis (%)	Femoropopliteal occlusion (%)
20 months	90	96	91	84
Maximum over 6 months	95	100	97	100
Maximum over 6 months (before glidewire)	90	100	89	89
Minimum over 6 months	84	94	78	72
Maximum over 2 months (before glidewire)	92	—	—	—
Minimum over 2 months	76	—	—	—

Thrombolysis in high risk patients

F. V. Gleeson, G. McGann, K. Dawson, A. Platts and G. Hamilton
Department of Radiology, The Royal Free Hospital, London NW3 2QG, UK

The advent of low antigenic thrombolytic agents with minimal systemic activity and small gauge catheters with good torque control enables thrombolysis to be used in patients who may previously have been deemed unsuitable. Thrombolysis may be used successfully in patients who are poor surgical candidates, or to reduce the extent of limb loss. Thrombolysis may be used in these patients despite conditions which were previously considered to be contraindications. The continued use of a thrombolytic may also be warranted despite an iatrogenic complication, *i.e.* extravasation, if the alternative is a major amputation. We report on a series of patients in whom tissue plasminogen activator was used successfully despite either recent surgery, or extravasation. Suggestions for the use of thrombolysis, in high risk patients, and following iatrogenic complications are discussed.

The use of isotope limb blood flow in the assessment of peripheral angioplasty

P. J. Thorley, K. L. Sheard and M. R. Rees
Radionuclide Department, Killingbeck Hospital, Leeds LS14 6UQ, UK

Isotope limb blood flow (LBF) measurements were performed to assess the outcome of peripheral angioplasty using balloon, laser and Kensey catheter techniques. Limb blood flow studies were carried out before angioplasty, and at 3 weeks, 3 months, 6 months and 1 year post angioplasty. Thirty-two of the laser angioplastied limbs were technically successful; of these, 22 (72%) showed an increase in LBF of greater than 20% (range 23–311%) at 3 weeks. The corresponding figures are 67% (21 successes) for the Kensey catheter and 47% (n=32) for balloon angioplasty. This increase in LBF was sustained at 6 months in a limited number of limbs: 33% of laser, 17% of Kensey, and 46% of balloon angioplasties. Even though a fall in LBF was frequently observed, presumably indicating the recurrence of disease, improvement in LBF between the pre-angioplasty and 6 month measurements was found in 5%, 53% and 38% of limbs for laser, Kensey and balloon techniques. Doppler pressure measurements gave very similar figures. A significant difference in LBF was seen only in two out of the 35 cases where both 6 and 12 month measurements were available, thus the more complete 6 month data set was used. Follow-up angiography was performed on 30 limbs. Concurrence with LBF results was seen in 28 limbs with a significant fall in LBF reflecting re-stenosis or occlusion, or the development of further significant disease.

A return to vasodilatation for demonstration of distal vessels

K. P. Gill, P. Grech and A. Al Kutoubi
Department of Diagnostic Radiology, St Mary's Hospital, Paddington, London W2, UK

The advent of better equipment and low osmolar contrast allowing improved opacification has led to a decreased interest in the pharmacological methods of enhancing arterial demonstration. However, bypass grafting to the infrageniculate vessels is now undertaken with increasing frequency and requires good visualization of the distal lower limb arteries. Intra-arterial vasodilators are known to be of value where poor visualization is due to spasm but they are not widely used in atherosclerotic disease. We report on our use of tolazoline to improve visualization of the distal leg vessels in patients with atherosclerosis. Tolazoline, 10 mg, was injected intra-arterially following an initial run demonstrating the popliteal trifurcation. Six minutes later the run was repeated, each patient acting as their own control. Improved visualization of the distal arterial tree was obtained in the majority of cases. Tolazoline is recommended as an adjunct to improved arterial demonstration where distal grafting is envisaged.

Evaluation of peripheral angioplasty using intra–arterial Doppler ultrasound

G. G. Hartnell, E. Berry, J. Willcox and R. Parry
Department of Radiodiagnosis, Bristol Royal Infirmary, Bristol BS2 8HW, UK

Angiography after percutaneous angioplasty (PTA) is a poor predictor of restenosis and successful long-term outcome. This may be because angiography demonstrates anatomy and is poor at assessing function. We have investigated intra-arterial Doppler ultrasound before and after PTA to determine whether this provides better assessment of functional response to angioplasty and to determine whether this gives useful prognostic information. The Doppler ultrasound examination is performed using a 20 MHz pulse wave Doppler catheter (Millar Instruments Inc.) mounted on a catheter which is 3 F at its tip. Doppler signals are analysed using a dedicated spectrum analyser (Dop Station, SciMed Ltd). Laboratory studies using a non-pulsatile flow phantom have demonstrated a consistent relationship between the measured and actual flow velocities. Doppler ultrasound measurements have been made in groups of patients having PTA for femoropopliteal stenosis/occlusions or graft related stenoses. The restoration of peak flow velocities of greater then 50 cm/s and return of a normal triphasic Doppler waveform has been associated with a good short-term prognosis. Initial evaluation of intra-arterial Doppler ultrasound suggests that this technique may provide useful information at the time of angioplasty to predict successful outcome and may be useful for risk stratification and determining frequency of follow-up.

Clinical application of intravascular ultrasound in arterial disease

P. J. Scott, A. R. Essop, M. R. Rees and G. J. Williams
Non-invasive Heart Unit and Cardiac Radiology Department, Killingbeck Hospital, Leeds LS14 6UQ, UK

Intravascular ultrasound (IVUS) is the latest of current vascular imaging techniques. Ten cases (seven peripheral and three coronary) undergoing balloon or laser angioplasty or Kensey catheter atherectomy were studied to define its clinical applications. A 20 mHz, rotating ultrasound transducer (Boston Scientific) was used which had the following characteristics: depth of field 10–12 mm; optimal focal distance 3.8–4.0 mm; lateral resolution 300–450 μm at the focal point. The results were as follows. Diagnostic applications are (i) the ability to diagnose intimal disease and its extent and/or depth (nine out of 10 cases), and (ii) tissue characterization of intimal disease, *i.e.* lipid-rich tissue versus fibrotic plaques or calcific deposits (nine out of 10 cases). Therapeutic applications are (i) accurate measurements of lumen diameter for balloon or stent size section, (ii) assessment of the effectiveness of intervention, (iii) measurement of residual disease following angioplasty or atherectomy, (iv) assessment of extent of complications such as dissection, and (v) selection of most appropriate intervention (laser versus atherectomy). Current limitations are (i) a long learning curve, (ii) relative inflexibility of catheters, (iii) sub-optimal depth of field for larger vessels such as aorta, (iv) lack of forward viewing, and (v) expense
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tions of this technique.

12.15 – 1.15

MacKenzie Davidson Memorial Lecture

Oxford Room

Advances in basic science – have they benefitted patients with cancer?

S. Dische
Marie Curie Research Wing for Oncology, Mount Vernon Hospital, Northwood HA6 2RN, UK

The trainee in clinical oncology is required to study physics, biology, medical statistics and pathology and to be tested by examination in these subjects. This knowledge of basic science is regarded as essential preparation for clinical practice. Trainees are encouraged to learn about advances in knowledge and if we look at the last 25 years there is much to be absorbed. For example, with bioengineering in physics we have greatly improved ways of imaging tumours – computerized tomography and magnetic resonance, positron emission tomography and isotope scanning. These give the possibility of greater precision in the planning of radiotherapy which can now be given with a high standard of quality control by new therapy machines. The monitoring of tumour response and the detection of recurrences and metastases has been greatly improved. In radiobiology there has been a large accumulation of knowledge, with the oxygen effect, cell kinetics, intrinsic radiosensitivity and hyperthermia being areas of particular endeavour. In statistics there has been development in the methodology of clinical trials and we have learned how to construct such studies in order to obtain meaningful results. Most recently, the overview has been introduced. In pathology, immunohistochemistry has increased the range of investigation and has led to greater precision in diagnosis and classification of tumours; there has been better recognition of prognostic factors influencing outcome. These advances have, to a greater or lesser extent, influenced the practice of clinical oncology, but consideration will be given to the benefits which may, or may not, have been achieved by patients and the prospects for the future.

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2.30 – 3.45

Radiological History

Clarence Room

The history of angiography

R. G. Grainger
Department of Radiology, Royal Hallamshire Hospital and Sheffield University, Sheffield S10 2JF, UK

The first arteriogram, a post mortem injection of calcium carbonate, was performed by Lindenthal in Vienna in early January 1896, a few days after Roentgen's original announcement. The first visceral post mortem arteriogram was (probably) injected in Sheffield and published a few days later. Clinical limb arteriography was introduced in Frankfurt and St. Louis in 1923, injecting strontium bromide and sodium iodide. Clinical carotid arteriography was first performed by cut-down injection of sodium iodide by Moniz in Lisbon in 1927, followed the next your by his colleague's (dos Santos) introduction of direct puncture lumbar aortography. Successful angiography requires selective injection of safe, painless contrast agents. These were progressively developed between 1927 and 1971, when low osmolar tri-odinated benzoic acid derivatives were introduced by Almen of Malmo. Selective catheterization of individual branch arteries was achieved by developments of the catheter wire-replacement technique introduced in 1953 by Seldinger in Stockholm. It is ironic that having achieved superb high definition, painless, selective arteriography throughout the body, recent imaging developments permit excellent arteriography with minimal contrast medium (digital subtraction angiography) and even without any contrast agent or selective catheterization (magnetic resonance imaging).

Historical experiments predating commercially available computed tomography

S. Webb
Joint Department of Physics, Institute of Cancer Research and Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT, UK

Computed tomography (CT) was a revolution in radiology. Commercially available CT scanners appeared in 1972, a joint effort between Sir Godfrey Hounsfield, the EMI Company, London's Atkinson Morley's Hospital and the DHSS. Many earlier experiments can, with hindsight, be considered precursors to CT. Gabriel Frank's patent in 1940 showed apparatus for back-projection CT and Takahashi developed equipment in the 1940s for reconstructing from a sinogram, in both cases using an optical "computer". A medical CT scanner was reportedly constructed in 1957 in Kiev. Transmission CT was performed by Kuhl in 1965. Cormack built an experimental scanner in 1963. Oldendorf identified what was needed for successful CT as early as 1960. A host of independent workers were busy on the mathematical problems of reconstructing from projections through the 1960s with both medical scanning and non-medical applications in mind. Experiments in early emission tomography influenced the development of CT. Even "classical" tomography, as started before 1920, came close to the realization of CT, with the pioneering British radiographer Watson standing out. This lecture is a thumbnail sketch of the origins of radiological CT. A fuller story is told in *From the Watching of Shadows: the Origins of Radiological Tomography*, Adam Hilger, Bristol, 1990.

The origins of radiological apparatus

W. D. Hackmann
Museum of the History of Science, Oxford, UK

One of the great advances of modern physics made during the closing years of the nineteenth century was the discovery of X-rays. This discovery occurred within the framework of contemporary theory and experimentation on the nature of electric discharges in gases at low pressure. Early researchers such as Plücker, Crooke, and Lenard must have produced X-rays accidentally while studying cathode rays, but only Röntgen appreciated that he was dealing with 'new kind of rays'. For X-rays to gain substance their existence had to be accepted by the scientific community, and this required that their properties had to be elucidated using existing laboratory apparatus. Röntgen called them X-rays because he felt that their nature was uncertain. Doctors were quick to see the benefits even before the physicists had settled their controversy whether they were dealing with particles or with waves. In this brief lecture we shall examine the three inter-related facets that made the early use of X-rays possible: (a) the experimental framework; (b) the development of the high-voltage Wimshurst and induction coil; and (c) the development of laboratory glass-blowing technology.

Seeing with sound: a medical adventure starting during the 1950s

R. van Tiggelen
Akad. Ziekenhuis/Military Hospital, Brussels, Belgium

All the early studies on diagnostic pulsed ultrasound were performed by personnel involved with military sonar and radar techniques. In 1942, Dr George Ludwig from the Naval Medical Research Institute (USA) was able to produce A-mode echography using discarded military equipment; he experimentally discerned gallstones and foreign bodies embedded in animal tissue. In 1952, another american physician, Dr Douglas Howry, used spare parts of Air Force radar equipment at a frequency of around 2–5 MHz together with a rotating ring from a B-29 bomber gun turret. All of this was immersed in a water tank and generated the first B-mode pulse echo scan. In 1962, Dr Ian Donald and engineer Ian Brown (Glasgow) produced a prototype of the first contact scanner. A different technique, called at that time (1951) "transducer in a can", which in fact happened to be the first clinically operational real-time scanner, was again designed by John Wild together with engineer John Reid. The same group also developed a whole range of ultrasonic transducers (transrectal and transvaginal). In 1953, the Swedish physician Dr Inge Edler and German physicist C. Hertz, simultaneously with a Japanese team led by Shigeo Satomura (which was working on Doppler echocardiography), developed a pulse echo motion mode echography for the study of the heart. Finally, the linear-array transducer was designed in 1971 by a Dutch team under the direction of Nicolaas Bom.

Reception of W.C. Roentgen's detection of X-rays in German and Austrian newspapers and journals

H.-J. Maurer
Radiology Unit, Faculty of Medicine, University of Malaya, 59100 Kuala Lumpur, Malaysia

Unusually for the time, Roentgen's detection of X-rays was published in the Viennese *Presse* in January 1896 before being published in *Sitz-Ber., Physikal-med. Ges., Wuerzburg*. This had been made possible because his friend the physicist Professor Zehnder of Prague, who had been informed by Roentgen himself, had passed on the news to his son, a journalist in Vienna, who published the sensational news in two articles in the Viennese *Presse*. Reuters of London immediately perceived its importance and cabled the news round the whole world. Investigation of German newspapers and journals from 1896 to 1901, the year Roentgen won the Nobel Prize, shows a large body of articles in 1896–1897 all with positive tenor. A waltz had been composed, caricatures drawn and a special chess play developed. Jokes and caricatures had been published in satiric journals, including the British *Punch*. Only a few rich people had been afraid of the discovery, fearing that thieves would screen flats, houses and safes to check the contents. During 1896 the articles became scarcer and more realistic and in the following years the number of articles diminished and they were more informative and technical. Roentgen's Nobel Prize attracted only short coverage. Since the unit Roentgen has been replaced by the Gray (radiotherapy) and Becquerel (diagnostics) his name will become less and less known, in spite of his detection having made modern medicine possible.

Perceptions of radiology in the management of diseases of bones and joints

J. M. Guy
Department of Radiology, Yeovil District Hospital, Yeovil, Somerset BA21 4AT, UK

The inherent contrast between bone and soft tissues provided the earliest operators of X-ray equipment with the inspiration to apply this new found technique to the diagnosis of fractures and dislocations. However, the technical limitations of such equipment and unexpected difficulties of interpretation discouraged some surgeons from relying on the new diagnostic method, and led to a reluctance to accept radiological diagnoses of more subtle diseases, such as infection and tumours. This is more apparent from the reading of surgical than radiological literature in the works written before the first World War. A comparison of surgical and radiological texts prior to 1940 reveals that the radiographs reproduced in surgical books are often of poorer quality than those found in radiological volumes. The surgeons seem to be using material which is inferior to the best available at the time. This may represent a lower expectation of the technique from the referring surgeon. It also indicates that the best radiography of the day has not always been available in any one hospital or at the time it was needed. The potential of new apparatus and methods had to be made clear not only to radiographers and radiologists but also to the doctors who sent patients to them. Such problems have more than purely historical relevance.

2.30 – 3.45

Are Radiotherapy Machines User-friendly?

Balmoral Room

Are radiotherapy machines user-friendly? – a physicist's view

J. B. Tuohy
Medical Physics Unit, Cookridge Hospital, Leeds LS16 6QB, UK

As radiotherapy treatment machines such as linear accelerators become progressively more complex, offering an expanding range of clinical facilities, an ever-increasing range of test procedures and systems have to be adopted to establish confidence in the performance of such equipment. Since such testing must form a fundamental part of safe radiotherapy practice, more thought could be given to incorporating in the equipment, features which would facilitate and expedite the process. In addition, all possible measures should be taken in the design of the machines, to facilitate service personnel in fault diagnosis and rectification, since downtime due to faults leads inevitably to treatment disruption and cancellation. This paper identifies some aspects of equipment design affecting both performance monitoring and servicing, which are not "user-friendly" and suggests some practical measures that might be incorporated to overcome the problems.

Are radiotherapy treatment machines user-friendly? – the radiographers' view

M. Granville-White
Department of Radiotherapy, Department of Clinical Oncology, General Hospital, Nottingham NG1 6HA, UK

Radiographers form part of the team responsible for the specification of radiotherapy equipment. As users of radiotherapy treatment machines they are well placed to provide a review and feedback mechanism complementary to experiences gleaned from their consultant radiotherapist and medical physicist colleagues. The content of this paper intends to review the response of manufacturers to the needs of users while touching on a few of the issues which could prevent radiographers within the teams from achieving their objectives.

Evaluation of metal-oxide-semiconductor field effect transistor detectors as radiation dosimeters for radiotherapy beams

M. Soubra, J. Cygler, *G. MacKay, *I. Thomson and A. Ribes
*Medical Physics Department, Ottawa Regional Cancer Centre and *Thomson and Nielson Electronics Ltd, Ottawa, Ontario K1Y 4K7, Canada*

A direct reading semiconductor dosimeter has been investigated as a radiation detector for photon and electron therapy beams of various energies. The operation of this device is based on the measurement of the threshold voltage shift in a custom-built metal–oxide–semiconductor field effect transistor (MOSFET). Within a certain dose range, the voltage shift of the linearity region increases with increasing bias voltage. The energy response of this detector is largely enhanced for low photon and electron energies. However, by incorporating an appropriate filter in the dosimeter, a much flatter energy response is achieved. The modes of operation give this device many advantages, such as continuous monitoring during irradiation, immediate reading and permanent storage of total dose after irradiation. The availability and ease of use of these MOSFET detectors make them very promising for use in clinical dosimetry.

Optimized three-dimensional treatment planning using a multi-leaf collimator

S. Webb
Joint Department of Physics, Institute of Cancer Research and Royal Marsden Hospital, Sutton, Surrey SM2 5PT, UK

A multi-leaf collimator (MLC) attached to a radiotherapy treatment machine can assist in achieving the aims of conformal radiotherapy, by giving a high uniform dose to an irregularly shaped treatment volume (TV) whilst sparing radio-sensitive structures. Several (preferably around 10–20) treatment fields are combined with the MLC open aperture shaped to the beam's eye view (BEV) of the TV.

The fields need not be coplanar nor be switched on for the same duration and the question arises of what is the optimum distribution of monitor units per field to achieve the best fit to a three-dimensional dose prescription. This problem has been solved by the numerical method known as simulated annealing. Starting from a uniform set, the field weights were randomly adjusted by small increments and at each such iteration the resulting three-dimensional dose distribution was compared with the three-dimensional dose prescription. The "thermodynamic rules" of simulated annealing were used to govern acceptance or rejection of changes, until, after many thousands of iterations, a set of weights has been derived delivering a dose distribution which is the closest possible to the prescription (a quadratic cost function was used). The method has been coded and implemented on a VAX 3900 computer and applied to model three-dimensional tumours of irregular shape with closely entangled sensitive structure. Most BEVs "see" both tumour and overlying or underlying sensitive structure and it would be impossible to determine the field-weights *ad hoc*. Typically, the optimum set of field weights leads to a distribution where the mean dose to the sensitive volume is about 10% lower than that from uniform weights, such results obviously being problem specific.

The advantages of proton beam radiotherapy

A. E. Nahum
Joint Department of Physics, Royal Marsden Hospital, Sutton, Surrey SM2 5PT, UK

The goal of conformal radiotherapy is to maximize the dose to the tumour while minimizing the dose to organs at risk. This should enable a higher dose to be prescribed to the tumour thus improving local control. Current attempts at conformal therapy using multi-leaf collimators etc. have been largely restricted to conventional megavoltage photon beams. The depth–dose characteristics of proton beams are vastly superior to those of photon beams, making protons much better suited to conformal therapy. Up to the present, clinical results with proton beams, primarily at Harvard, have demonstrated their superiority for treating ocular melanomas, chordomas and chondrosarcomas. Recent developments in accelerator technology now enable beams of sufficiently high energy (250 MeV) to be produced and delivered from an isocentrically mounted gantry, as at the recently opened facility at Loma Linda, CA. Examples are presented of the vastly improved sparing of normal tissues even for deep-seated tumours in the pelvis, where significant improvements in local control for large numbers of patients can be expected if proton beams are employed.

Evaluation of a radiotherapy electronic portal imaging device

C. Nalder, T. Greener, C. Baldock and J. Saunders
Medical Physics Department, St Thomas' Hospital, London SE1 7EH, UK

Verification of the correct radiation beam position with respect to the patient's anatomy is important for all radiotherapy treatments. A portal image of the beam is often taken at the first treatment session using conventional radiographic film to confirm accurate set up. Recently matrix ionization chambers suitable for obtaining digital images have become commercially available. A scientific and clinical evaluation of such an electronic imaging device recently installed in the South East London Radiotherapy Centre at St Thomas' Hospital was undertaken. This involved making comparisons with existing techniques used in the department. We present results of the scientific evaluation comparing measurable image quality parameters such as contrast detail and resolution. The clinical evaluation was made taking advantage of the pseudo real time images that can be obtained to examine intra-treatment motion and the efficiency of current immobilization techniques.

A rectal applicator for use with a selectron

R. Orpwood, A. Gammie and *G. Rees
*Bath Institute of Medical Engineering, Royal United Hospital, Bath BA1 3NG, and *Radiology and Oncology Centre, Bristol Royal Infirmary, Bristol, UK*

This paper describes an applicator for use with the selectron after-loading radiotherapy equipment to enable treatment of rectal tumours. Two applicators have been developed, consisting of polypropylene enclosures into which three tubes are mounted to accept the selectron pellets, and with end fittings to suit the selectron tubes. One of the applicators has a removable nose which allows lead shielding to be inserted to generate non-radially symmetrical distributions. The main problem with rectal applicators is to hold them securely in position during treatment. The problem has been solved in our device by using disposable air-filled latex balloons. The balloons are moulded to fit around the polypropylene applicators and lock them in position when inflated by clamping either side of the anal canal. In order to maintain the balloons in an inflated state throughout the treatment period they are connected to a small air pump. The pump is controlled by a pressure controller that keeps the balloon pressure around 75 mm Hg. Appropriate alarms are fitted outside the treatment room to give indication of excess pressure changes. Six patients have been treated so far. The device has been well tolerated and the clinical results have been very encouraging indeed.

One year's experience with the first Therapax series 3 superficial treatment unit

H. M. Morgan and S. M. Smith
Wessex Regional Medical Physics Service, Royal United Hospital, Bath BA1 3NG, UK

This unit was installed in December 1989 as a replacement for a KX-10 superficial unit. The energies available on the KX-10 had half-value layer (HVL) values of 1 mm, 3 mm and 8 mm of aluminium, and a similar range was a requirement for the replacement unit. The Therapax unit comprises a metal ceramic X-ray tube with high frequency generator and a microprocessor control system. Eight filter – milliamp – kilovolt combinations are available for clinical use. This paper describes the acceptance testing and the compliance of the unit with radiation safety standards. Beam characteristics for energies in the HVL range 1 – 12 mm aluminium are described and depth – dose data are compared with those already published. Values of backscatter factors measured for the range of applicators supplied are compared with the current literature. Since the unit has been in clinical use, radiation output measurements have been performed daily and they demonstrate the stability of the treatment unit's radiation output. Minor problems have occurred during the first year, predominantly owing to the prototype software, but otherwise the Therapax has proved itself a worthy replacement for the KX-10 treatment unit.

Notes

2.30 – 3.45

Teach-in: Modern Gynaecological Treatment Planning

Lancaster Room

R. D. Hunter
Christie Hospital, Wilmslow Road, Withington, Manchester M20 9BX, UK

Treatment planning for radical radiotherapy in carcinoma of the cervix has always been based on inadequate information and, as a result, has been dominated by large overall external beam therapy given to overall pelvic tolerance supplemented by standard intracavitary techniques. The advent of improved imaging and modern collimation techniques promises to change this situation radically. For external beam planning there is a requirement for better knowledge of the primary tumour volume and the presence of early lymph node involvement. A prospective MR scanning project (involving more than 120 patients) shows enormous promise with regard to the more accurate definition of the primary tumour volume and the detection of significant early lymph node enlargement. This information can be used in planning the external beam fields which can be shaped individually using multileaf collimator techniques so reducing the target volumes considerably. For the intracavitary therapy phase very useful information can be obtained using CT scanning of patients with afterloading applicators in position. This has enabled unexpected uterine perforation to be identified in 3% of cases. It has also given information about uterine myometrial thickness and the relationship of the applicators to bladder and rectal/sigmoid which has resulted in modification of dose distribution in approximately 25% of patients. The impact of these new emerging techniques based on modern technology to routine radical pelvic radiotherapy for carcinoma of the cervix remains to be established by prospective study but the tools are now available and the age of "blind" treatment planning is potentially at an end.

Notes

2.30 – 3.45

Doppler Ultrasound

Norfolk Room

Doppler ultrasound, duplex scanning and colour flow mapping

J. P .Woodcock
Medical Physics and Bioengineering, University Hospital of Wales, Cardiff CF4 4XW, UK

The Doppler shift signal from a blood vessel contains information about the velocity distribution across the blood vessel, and the way this varies with time over the cardiac cycle. In general, it is true that each artery seems to have its own typical Doppler-shift spectrum and that this typical spectrum can be changed by disease, either of the vessel itself, as in atherosclerosis, or by the tissue bed fed by the vessel *e.g.* tumours, renal transplants. It is important to recognize there these typical Doppler spectra and then to use this information to characterize functionally, the distal vascular bed. This basic philosophy has proved to be particularly useful in the study of the transplanted kidney where the early signs of acute rejection are an increase in the impedance presented by the kidney to the transplanted renal artery, and in studies on the overactive thyroid. Duplex ultrasound has also proved extremely useful in the study of solid lesions by providing information on the lesion's vascularity. This has been shown to be useful in the study of primary hepatocellular carcinoma and liver metastases, as well as in the study of carcinoma of the breast, cutaneous melanoma, and sub-mandibular masses. The advent of colour flow mapping has greatly increased the usefulness of clinical Doppler ultrasound because (1) it allows an overview of perfusion – is there an area of tissue which is not well perfused? (2) it speeds up the investigation, because Doppler information can by displayed from the whole tissue plane, in real-time; (3) it indicates flow direction, which is extremely useful after various surgical procedures such as spleno-renal shunts, and porta-caval shunts; (4) it identifies small blood vessels which then can be studied by investigation of the Doppler spectrum; (5) high velocities and/or aliasing are displayed immediately; and (6) it shows the relationship of high velocity blood flow areas to the underlying pathology. Colour flow map systems present important data such as high velocities, spectral broadening, and boundary layer flows, as a function image superimposed on the more usual anatomical information. This brings the whole area of Duplex ultrasound more readily into the area of radiology, and will greatly enhance the clinical acceptance of these techniques, as a result.

Comparison of colour Doppler ultrasound with venography in central vein thrombosis

G. M. Baxter, W. Kincaid, R. F. Jeffrey, G. M. Millar, C. Porteous and P. Morley
Department of Radiology, Western Infirmary, Glasgow G11, UK

Colour Doppler ultrasound is a new technique that has recently been shown to be a suitable alternative to venography in the diagnosis of lower limb venous thrombosis. In view of this, and in order to see if this technique is applicable to the diagnosis of central vein thrombosis, we performed a double blind prospective trial on 19 renal dialysis patients (30 limbs), all of whom had had multiple central venous cannulations. Both colour Doppler and venography were done in all cases, these investigations being within 2 hours of each other and performed by different radiologists. Colour Doppler ultrasound was as accurate as venography, with complete correlation between both techniques in the diagnosis of venous occlusion. A case of subclavian vein stenosis was missed using colour Doppler as it lay directly beneath the clavicle and was thus an ultrasonic blind spot. Apart from the obvious advantage of safety and financial saving, colour Doppler gave more information on the local extent of thrombus within the internal jugular and innominate veins, this information often being absent on venography. In addition, it is a quicker technique than Doppler ultrasound alone and has the advantage of visualizing collateral vessels, adding confidence to the diagnosis.

Venous ultrasound in the thigh: normal variants and potential pitfalls

G. R. J. Sissons and N. D. Pugh
Department of Diagnostic Radiology, University Hospital of Wales, Cardiff CF4 4XW, UK

Sonography is a useful technique in the diagnosis of femoropopliteal venous thrombosis. Compressibility studies are the mainstay of diagnosis. Duplex and colour flow Doppler provide additional information though their exact role remains to be established. Thirty-six volunteers with no history and few risk factors for venous thrombosis were studied with duplex and colour flow Doppler equipment. A variety of normal variants are presented. In particular, duplications of the superficial femoral vein are seen in approximately 20% of individuals, a figure much higher than that quoted in many anatomical surveys. This is a potential source of error in suspected venous thrombosis when only one of the vessels may contain thrombus. Focal areas of incompressibility may also be seen at certain sites, particularly in the profunda femoris vein and at the adductor hiatus. By demonstrating normal vascular "fill-in", colour flow provides additional information that cannot be obtained with real-time B mode or duplex studies alone and its advantages are discussed.

The value of duplex Doppler in detecting hepatic artery thrombosis following liver transplantation

R. Wellings, S. Olliff, J. Olliff, *M. Deakin, +H. Alton and *P. McMaster
*Department of Radiology and *Liver Unit, Queen Elizabeth Hospital, Birmingham B15 2TH and +Department of Radiology, Children's Hospital, Birmingham, UK*

Following orthotopic liver transplantation, hepatic artery thrombosis is a potentially life threatening complication. Fulminant hepatic failure and donor biliary complications may result. In our experience, retransplantation is often required. Duplex Doppler ultrasound offers a non-invasive bedside technique to detect this complication. Angiography is too complex a procedure for screening but provides confirmation of the diagnosis. We aim to determine the accuracy of duplex Doppler in detecting hepatic artery thrombosis during the early post-operative period. The patients are examined on the first and seventh day after transplantation and otherwise as clinically directed. If no satisfactory hepatic artery signal is found, the scan is repeated within 24 hours. If there is still no satisfactory signal, angiography is performed. It is important that both the ultrasound examination and angiography are performed with knowledge of the vascular anastomosis anatomy, as hepatic arterial anomalies are common. Forty-eight patients have been examined. Five cases of confirmed thrombosis have been detected by ultrasound. In three further cases, angiography demonstrated patent hepatic arteries. No patient with thrombosis has yet been said to have a patent vessel on ultrasound. Overall results will be presented and discussed.

Umbilical artery Doppler ultrasound in the antenatal assessment of the growth discrepant twin pregnancy

S. J. Stinchcombe and P. Twining
Department of Radiology, Queen's Medical Centre, Nottingham NG7 2UH, UK

There is an increased incidence of perinatal morbidity and mortality in twin pregnancy which is either due to prematurity or to growth discrepancy. Severe growth discrepancy is associated with a high perinatal mortality and a low subsequent I.Q. whereas mild growth discrepancy is usually associated with a good perinatal outcome. Doppler ultrasound of the umbilical arteries was carried out in 25 twin pregnancies in which there was clinical or ultrasonographic suspicion of growth discrepancy. Umbilical artery systolic:-diastolic ratios (A/B ratios) were measured close to the fetus and the examination was repeated every 2 weeks up until delivery. There was a very strong negative correlation between the A/B ratio and the subsequent birth weight (R=0.85). There was a strong positive correlation between the intertwin A/B ratio difference and the intertwin birth weight difference (R=0.7). An intertwin A/B ratio difference of more than 0.5 was strongly associated with severe growth discrepancy (P<0.01). There was a strong association between an elevated A/B ratio and a poor perinatal outcome (P=0.01). Absent or reversed diastolic flow were extremely poor prognostic findings. The results indicate that umbilical artery Doppler ultrasound is of value in the antenatal assessment of growth discrepancy.

Duplex Doppler ultrasound: an easy, non-invasive way to detect alterations in renal blood flow during infusion of dopamine

I. Mastorakou, *D. Young, +J. Firth, D. Lindsell, *C. Garrard and +J. Ledingham
*Department of Radiology, *Intensive Care Unit and +Nuffield Department of Medicine, John Radcliffe Hospital, Oxford OX3 9DU, UK*

Duplex Doppler ultrasound is widely used to estimate organ blood flow. In the kidney, direct measurement has proved difficult, especially when perfusion is unstable. We have investigated the changes in resistive index (RI) and pulsatility index (PI) by duplex Doppler ultrasound, in response to intravenous dopamine. Fourteen subjects, four healthy volunteers (group I) and 11 patients in intensive care were examined. Seven of the patients (group IIa) had impaired renal function. The other four patients (group IIb) had normal renal function. The peak systolic, end diastolic and mean velocities were measured from the waveform of an interlobar artery and PI and RI were calculated at rest as a baseline study (PI1, RI1), after infusion of dopamine at 2.5 μg/kg/min (PI2, RI2) and 5 μg/kg/min (PI3, RI3). The mean indices (±SD) were as follows:

Group I
RI1=0.597(0.031) RI2=0.567(0.012) RI3=0.593(0.032)
PI1=1.037(0.065) PI2=0.917(0.070)* PI3=1.090(0.098)
Group IIa
RI1=0.740(0.028) RI2=0.727(0.017) RI3=0.745(0.024)
PI1=2.180(0.166) PI2=2.056(0.392)* PI3=2.310(0.690)
Group IIb
RI1=0.678(0.059) RI2=0.658(0.061) RI3=0.668(0.078)
PI1=1.457(0.239) PI2=1.438(0.328)* PI3=1.513(0.371)

(*Significantly reduced ($p<0.05$) compared with baseline: paired T-test.)
Alterations in RI and PI have been taken to reflect alterations in vascular resistance, a fall correlating with reduction and *vice versa*. It has already been shown that dopamine at 2.5 μg/kg/min increases renal perfusion in healthy subjects. Similar changes in PI produced by dopamine in both patients and normal controls provides some new evidence that this also occurs in renal impairment. It was also demonstrated that the mean values of both RI and PI were higher in patients than in normals, suggesting that renal vasoconstriction may occur in intensive care unit patients with normal renal function.

Doppler ultrasound of renal artery blood flow following transplantation: how reproducible are the measurements?

J. M. Fields and P. M. Taylor
Department of Diagnostic Radiology, University of Manchester, Manchester M13 9PT, UK

Several recent studies have documented the value of duplex Doppler ultrasound in the assessment of complications following renal transplantation. None has addressed the problem of reproducibility of measurement. The aim of this study was to assess the intraobserver and interobserver variation in the measurement of flow in the transplanted renal artery. Twenty patients were studied. All had received transplants between 6 months and 5 years previously and were considered clinically and biochemically stable. Two independent observers examined the patient on two separate occasions. A commercially available system (Acuson 128) was used with a 5 mHz linear array probe. Measurements of the maximum systolic and diastolic flow velocities were made at a fixed distance from the iliorenal anastomosis. Measurements were not displayed to the observer at the time of investigation but were available for subsequent analysis. Significant intraobserver variation was demonstrated but this was less than the interobserver variation. The findings of this study suggest that longitudinal assessment of patients should be performed by a single observer and several measurements should be performed to obtain mean values.

Colour Doppler and cavernosometry in the evaluation of impotence

*S. Hampson, D. Kessel, D. Rickards and W. R. Lees
*Departments of *Urology and Radiology, The Middlesex Hospital, London W1N 8AA, UK*

Colour Doppler (CD) and cavernosometry (CVM) are used in the evaluation of impotence. However, the information obtained on venous incompetence (VI) by CD is questionable in the presence of arterial insufficiency (AI) and similarly CVM gives little information about AI in the presence of VI. Patients with uncertain diagnoses, mixed AI and VI and those requiring surgery should be investigated with both modalities. Eleven patients (mean age 53, range 27–70) are reported. Colour Doppler and CVM were performed independently by consultant staff not knowing the diagnosis in the alternate modality. Four different diagnoses were possible, AI or VI, a combination of both, or a normal response. Complete agreement was obtained in four patients (three VI, one AI). The diagnosis was modified in four patients. Two diagnoses of VI made by CD and two of AI made by CVM were changed to mixed AI and VI after examination in the other modality. In three patients there was total disagreement. In one patient a diagnosis of VI by CD was shown to be inaccurate because papaverine was not injected into the corpora. A normal response was subsequently obtained with CVM. One patient with a diagnosis of VI (and diastolic flow of 11 cm/s) gave a normal response on CVM and a diagnosis of AI made on CD was found to be normal on CVM. Both these results have been reviewed and are valid. It may be relevant that both occurred in patients with high anxiety levels. We would suggest that papaverine stimulation studies be interpreted with caution in such patients and conclude that the greatest accuracy in the diagnosis of impotence will occur when more than one investigative modality is used.

Duplex Doppler ultrasound in the investigation of occult nephropathy following the haemolytic uraemic syndrome

F. V. Gleeson, M. Fitzpatrick, J. Somers, C. Kennedy, R. DeBruyn and M. Barratt
Department of Radiology, The Hospital for Sick Children, Great Ormond Street, London WC1, UK

Duplex Doppler ultrasound has been reported to be of value in the detection of raised vascular resistance, particularly in the renal tract. A prospective single blind study investigating the use of duplex Doppler ultrasound in patients with impaired renal function and a past history of the haemolytic uraemic syndrome was performed for the following groups: group 1, normal; group 2, patients with mild renal impairment but a glomerular filtration rate greater than 80 ml/min per 1.73 m^2; group 3, patients with marked renal impairment and a glomerular filtration rate less than 80 ml/min per 1.73 m^2. The three groups were age and sex matched, and each contained eight patients. The resistive index (RI) calculated as the peak systolic blood flow velocity minus the minimum end diastolic blood flow velocity all divided by the peak systolic blood flow velocity, was taken from an average of five measurements on each kidney performed by two experienced observers. The RI in the three groups showed no significant difference: group 1, mean 63.4%, range 48.6 – 75.9%; group 2, mean 57.1%, range 47.4 – 65.0%; group 3, mean 57.1%, range 47.0 – 78.1%. We feel that the RI as determined by duplex Doppler ultrasound is of no value in predicting the likelihood of occult nephropathy following the haemolytic uraemic syndrome.

Is there a place for colour Doppler ultrasound in the assessment of retrobulbar eye flow?

G. M. Baxter, T. Williamson, G. McKillop, G. Dutton and P. Morley
Department of Radiology and Ophthalmology, Western Infirmary, Glasgow G11, UK

Colour Doppler ultrasound is a non-invasive method of blood flow analysis. As this technology has become available it has become apparent that it may have many useful applications. In view of this, we performed a prospective trial to see if colour Doppler ultrasound could reliably and reproducibly measure retro-orbital blood velocity parameters in 20 normal healthy volunteers. We assessed all velocity waveforms in the supine, sitting and erect positions and took three regional measurements within the orbit in all of the above positions. Results showed that there were significant regional variations of blood velocity patterns ($p < 0.001$) within the eye, independent of the spectral analytical parameter used. In addition, there was no significant change in these velocity waveforms, despite a change in posture, resulting in a small, but significant, rise in diastolic blood pressure and pulse rate ($p < 0.05$ respectively). We feel that these results show that Doppler ultrasound of the eye is an accurate, non-invasive method of assessment of retro-orbital blood flow patterns and its reliability in detecting significant regional flow variations may be a useful tool in the detection and management of certain eye diseases.

Notes

2.30 – 3.45

Techniques and Technology in Magnetic Resonance

Dukes Suite

The clinical potential of rapid T_1 mapping of the brain using multislice IR echo planar imaging

*B. S. Worthington, P. Gibbs, R. Coxon, M. Symms, P. Gowland and P. Mansfield
*Departments of Physics and *Radiology, University of Nottingham, Nottingham NG7 2RD, UK*

The use of relaxation time values in clinical practice has been inhibited by the level of uncertainty surrounding estimates derived from scanning techniques arising out of inherent tissue heterogeneity and systematic errors in measurement. This is particularly so when, because of time constraints, as few as two points on the magnetization relaxation curve are sampled. Echo planar imaging (EPI) techniques can be used to obtain accurate quantitative T_1 information in a very short time, allowing reappraisal of its value in clinical diagnosis. For this purpose both a single slice and a more time efficient multi-slice IR-EPI technique have been developed; the latter can generate T_1 maps of eight contiguous slices based on sampling eight points of the magnetization curve in approximately 30 seconds. The method allows for correction of incomplete spin inversion which may be caused by r.f. field inhomogeneity. High quality T_1 maps have been produced in a wide range of intracranial pathology and these are displayed using a colour scale which allows rapid identification of bands of T_1 values. The maps are studied in conjunction with conventional inversion recovery images which provide corresponding morphological information.

Clinical use of anisotropically restricted diffusion in magnetic resonance imaging of the nervous system

G. M. Bydder, J. V. Hajnal, M. Doran and I. R. Young
Nuclear Magnetic Resonance Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0NN, UK

Pulsed gradient spin echo (PGSE) sequences were used to provide images with diffusion weighted contrast. When the direction of the sensitizing gradients is varied, white matter tracts are selectively highlighted owing to the greater restriction of diffusion of water across myelinated fibres than along them. Twenty patients with a variety of neurological disease have been studied. Using a magnetic resonance (MR) system operated at 0.15 T, cardiac gated PGSE sequences with TEs of 130 or 200 ms, diffusion times of 44 or 103 ms and diffusion attenuation factors of 550, 1100 and 1510 s/mm^2 were employed in coronal, sagittal and transverse planes. Images unlike any previously seen with MR imaging were produced in all patients. Long and short association fibres and projection pathways were selectively highlighted. High signal areas of probable pathologic significance were demonstrated in cases of multiple sclerosis, radiation damage, AIDS and other diseases in areas of white matter where conventional imaging was normal. Anisotropically restricted diffusion (ARD) imaging, as described in animals, promises to have important clinical applications in lesion localization and improving sensitivity and specificity in central nervous system disease.

The determination of feature length from magnetic resonance image data

N. Roberts, C. V. Howard, L. Cruz-Orive and R. H. T. Edwards
Magnetic Resonance Research Centre, The University of Liverpool, Liverpool L69 3BX, UK

A new stereological method for determining feature length from total vertical projections (TVPs) will be described, and results from its applications to data produced by a whole body magnetic resonance (MR) imaging system will be presented. Length determination from MRTVPs of a twisted water-filled glass rod of known dimensions agree to within 1% of the true value. This was the case whether the MRTVPs were generated by rotating the specimen or through control of orthogonal gradients within the scanner. Magnetic resonance TVPs were also obtained of a living bonsai tree. The subsequent stereological determination of the total branch length of the tree is in good agreement with the value obtained from a series of photographs of the tree. The clinical utility of the method is exemplified by the determination of the length of the splenic vein, and the Circle of Willis, from projection MR angiography data obtained of an adult male. Stereological determinations of feature volume and surface area from MR image data are subject to biases introduced by over-projection effects. A bias in the length determination method can occur as the result of masking. The importance of this effect will be discussed.

A review of parameterization in magnetic resonance imaging for performance evaluation

J. P. Bean, K. Straughan and *J. A. Lunt
*Department of Electrical Engineering, Imperial College, London SW7 2BT and *Medical Devices Directorate, Department of Health, London, UK*

Magnetic resonance imaging (MRI) is a complex medical imaging modality and the performance assessment of the MRI system generates a vast amount of technical data. These data need interpretation for several objectives such as intersystem comparison, acceptance testing and quality assurance. The evaluation of a system involves quantifying the properties of a signal, contrast and noise. It includes measuring the image quality factors of spatial resolution, geometric distortion and uniformity. Furthermore, slice characteristics must be assessed such as slice warp, slice profile and slice position. The assessment of MRI is further complicated by its unique properties. This involves the quantitative measurement of the relaxation rates T_1 and T_2 and the evaluation of fast imaging and multislice imaging techniques. The philosophy of this research group is to develop and utilize sophisticated image processing techniques which parameterize the above technical factors, providing clear system performance information for interpretation by every level of expertise. The paper will present this approach with a review of image quality parameterization. It will emphasize exemplar advances in signal and contrast evaluation and the assessment of image artefacts such as ghosting using frequency domain analysis. The value of this assessment methodology will be illustrated with data collected from a variety of commercial MRI systems.

Alterations in contrast in magnetic resonance imaging produced by saturation transfer and spin locking techniques

C. J. Baudouin, D. J. Bryant and I. R. Young
Nuclear Magnetic Resonance Unit, Hammersmith Hospital, London W1N 0HS, UK

Saturation transfer is a technique in which saturating r.f. pulses, offset in frequency, are applied with normal imaging sequences. We have investigated the effects of such sequences on tissue contrast in order to develop sequences for clinical use. The effect of a spin locking pulse for a $T_1\rho$ experiment has been similarly studied. Imaging was performed at 0.15 T. Saturation transfer sequences consisted of an r.f. pulse of variable duration, 0.5–20 kHz off resonance combined with partial saturation, spin echo or inversion recovery sequences. In the $T_1\rho$ sequences a spin locking pulse of 70 ms was applied with a maximum r.f. field of 0.27 (lower than optimal). Alterations in signal and relaxation times were observed in the limbs of volunteers. Saturation transfer sequences caused a reduction in muscle signal still present at 20 kHz offset. T_2 measurements showed a rather more than doubling of the apparent T_2 of muscle. Effects on fat were less but still substantial. $T_1\rho$ sequences showed only small signal changes over the r.f. field range used. Initial studies in patients with osteosarcoma and soft tissue injury suggest contrast changes are seen in pathological areas using both saturation transfer and $T_1\rho$ techniques with marked changes in some cases with the latter, in spite of the r.f. field being limited. We feel these techniques are potentially useful in clinical studies.

A rapid and accurate multipoint imaging measurement of T_1 relaxation times using the TOMROP sequence

M. O. Leach and P. A. Gowland
Joint Department of Physics, Royal Marsden Hospital and Institute of Cancer Research, Sutton SM2 5PT, UK

TOMROP is a multireadout inversion recovery sequence with the potential to measure multicomponent T_1 relaxation recoveries *in vivo*. The method has been shown to be efficient in operation, allowing a much more rapid multipoint measurement than had been practicable with multipoint sequences. However, results reported in the literature have demonstrated poor accuracy and reproducibility, with the best results to date having systematic errors of 7–8%. By employing (a) a hyperbolic secant inversion pulse to provide an improved inversion, (b) a simple polarity restoration scheme allowing a simple non-linear fit to the data points, (c) an asymmetrical spoiler gradient scheme to destroy coherent transverse magnetization following each gradient echo, and (d) a fitting procedure that takes account of the read-out slice profile, the systematic error has been reduced to less than 1% with reproducibility of 1.2% in four measurements over a period of 1 month (T_1 values from 0.2–1.6 s).

Further developments of high temperature superconducting receiver coils

A. S. Hall, *N. Mc. N. Alford and I. R. Young
*Nuclear Magnetic Resonance Unit, Hammersmith Hospital, London W12 0HS and *ICI Advanced Materials, Runcorn, Cheshire, UK*

The possibility of using superconducting receiver coils has been substantially enhanced by the availability of high temperature superconducting materials which operate at liquid nitrogen temperatures rather than those of liquid helium. As has been shown previously, in a small bore machine the filling factor of a helium cooled coil was so reduced that it outweighed the thermal noise advantages of operating the coil at low temperature. This problem is less significant in a whole body machine, and with operation at liquid nitrogen temperatures. We have been studying surface coils formed from Y—Ba—Cu—O and mounted in an insulated chamber made of closed cell plastic with a wall thickness of 20 mm, and have demonstrated that we can obtain images *in vivo*. However, the magnetic properties of the solid filament wire we used in the original experiments were non-ideal, so that a superconducting coil with Q of 2500 in the earth's magnetic field showed a drop to 1700 at 0.15 T (and as such did not give a significantly improved performance over a similar coil made of copper operated at the same temperature). We have been developing thick film technology with the raw paste which is fired to produce the superconducting layer deposited onto a zirconic substrate. The principal mechanical problem in this form lay in the development of a way of bridging the inside end of the spiral coils to the outside. This has now been solved and we are in a position to begin trials of the new structures.

Localized spectroscopic T_1 relaxation time measurements using a two point IR/SR sequence

N. M. Yongbi, M. O. Leach, G. S. Payne and D. J. Collins
Joint Department of Physics, Royal Marsden Hospital and Institute of Cancer Research, Sutton SM2 5PT, UK

Previously, we have demonstrated that accurate T_1 relaxation time image maps can be obtained efficiently using an interleaved IR/SR sequence with a hyperbolic secant inversion pulse. We have adapted this technique for localized spectroscopic measurements by developing a two point ISIS measurement sequence, where the SR sequence is provided by the modified three-dimensional ISIS sequence, using selective hyperbolic secant pulses and an adiabatic half passage readout pulse. The IR sequence is preceded by a non-selective hyperbolic secant inversion pulse. T_1 values are calculated from the ratio of IR/SR signal amplitudes for a given spectral peak, by means of a look-up table. The method has been implemented on a Siemens 1.5 T whole body imaging and spectroscopy system. Localized proton measurements have been performed on a range of water phantoms doped with different concentrations of gadolinium, to provide T_1 values in the range 400–2500 ms. The measured T_1 values are within 6% of the calibrated values. Preliminary localized phosphorus measurements on calf muscle from three volunteers give the following results (in seconds): Pi, 3.7, 4.3, 3.8; PCr, 6.6, 6.5, 6.5; gamma-NTP, 3.8, 4.5, 4.9; alpha-NTP, 3.4, 3.5, 3.1; beta-NTP, 4.2, 4.4, 4.3. These results are in good agreement with those previously obtained by multipoint measurements. *In vivo* tumour measurements are currently in progress.

The role of performance assessment in the selection acceptance and quality assurance of magnetic resonance imaging

*J. A. Lunt, J. P. Bean, *J. Williams and K. Straughan
*Department of Electrical Engineering, Imperial College, London SW7 2BT and *Medical Devices Directorate, Department of Health, London, UK*

The performance assessment of magnetic resonance imaging equipment is a necessary exercise for the following three objectives: type testing, acceptance testing and routine quality assurance. The paper discusses the philosophy behind each evaluation task. It establishes the level of testing each objective requires and emphasizes the need to perform all three exercises. The evaluation tests can be categorized in a hierarchy of complexity. At the lowest level there are the tests that can be performed daily by the medical physicist. These are the essential quality assurance tests that can be undertaken with the equipment and software supplied by the manufacturer. The next level in the hierarchical tree would involve a more detailed assessment establishing that the equipment performs to the manufacturer's specification. This stage, although more rigorous, requires a pragmatic approach to the analysis. The top level would be a complete system evaluation involving the use of sophisticated image processing techniques for full image quality parameterization. This would be the objective for type testing and would require specialist software, as developed by the Imperial College research team.

Installation and initial experience of operating a 0.2 T permanent magnet magnetic resonance imaging system

R. Bodley and P. Savage
Department of Radiology, Stoke Mandeville Hospital, Aylesbury HP21 8AL, UK

Following the decision to proceed with the installation of the Hitachi MRP-20 0.2 T permanent magnet magnetic resonance imaging (MRI) system, it was 5 months to the official opening. This speed was greatly facilitated by the very compact magnetic field footprint of the unit and its lack of requirement for a separate complex air-conditioned computer room. As the control room and gantry room are together no bigger than a small computed tomography (CT) suite, is was possible to divide the Radiology Department waiting room in half and so install the unit within the current department, obviating the need for expensive special buildings, extra personnel and maintenance etc. Some of the problems involved in commissioning, design of room layout, sub-contractor interrelationships and the need for very clear documentation of all decisions made will be presented briefly. The requirements for radiographic staff and other supporting staff will also be discussed. As the machine is very easy to use, all staffing has been from within our current pool and, following a series of rotations, most senior staff in the department are now competent at straightforward examinations. Given our current financial situation, this was the only possible option, but it has, however, been extremely successful. The simplicity of the console renders MRI rapidly accessible to most radiographers with CT experience. A brief discussion of the imaging sequences available and some of our clinical results from the first 9 months of operation will be presented. We strongly believe that MR is affordable at District General Hospital level using machines such as this and some relative costings will be presented comparing MRI, CT and other screening examinations.

Notes

Some effects of prolonged r.f. irradiation

I. R. Young, C. J. Baudouin and D. J. Bryant
Nuclear Magnetic Resonance Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0NN, UK

It has been observed that prolonged off resonance r.f. irradiation introduces a variety of effects including line-narrowing, a complex saturation recovery pattern and, potentially, changes in the apparent T_1 of signals where cross-relaxation between the main free water and other proton pools is occurring. Since the effects are substantial in many tissues, the potential exists for the use of these pulses as a deliberate strategy for varying contrast. Line narrowing occurs in the rotating frame as $3\cos^2\Theta-1\rightarrow0$. where $\tan\Theta=\gamma B_1/\gamma\Omega$ and $\delta\Omega$ is the frequency offset of the r.f. field. Recovery from saturation follows the relation $\{1+(T_1/T_2)\tan^2\Theta\}^{-1}$. The effective value of T_1 in these circumstances is affected by cross-relaxation, if present, and can be observed using a PS/IR experiment in the presence of prolonged r.f. excitation. The effect on T_1 is given by $T_1=(M_{rfo}/M_{rf})$ where M_{rfo} is the observed magnetization in the absence of r.f. excitation, and $T_{1\ APP}$ is T_1 calculated in the presence of r.f. excitation. The variations observed (including for example line narrowing of 60% in muscle) offer the possibility of complex contrast manipulation, and the changes to be expected are discussed with illustrations.

4.15 – 5.30

Techniques and Technologies: Diagnostic Imaging

Clarence Room

Preliminary Experience with Ultrasound Contrast Agents

P. N. Burns
Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, PA 19107, USA

The detection of flow in small blood vessels using ultrasound Doppler is limited by two factors. First, the velocity of blood must be sufficient to produce a Doppler shift frequency that is distinguishable from that produced by the normal motion of tissue and, second, the received intensity of the backscattered ultrasound must provide adequate signal strength for detection. In deep vessels of the abdomen, the second limitation defines the smallest vessels from which Doppler signals can be detected. This presents a barrier to the characterization of such small vessels as those associated with the neovascularization of malignant tumours, whose detection with Doppler may help in the differential diagnosis of a solid lesion in soft tissue. There is, then clear clinical potential for a method capable of enhancing acoustic backscatter from moving blood, especially in the systemic arterial system. Although the first reported use of gas as an ultrasound contrast agent was as early as 1968, the clinical utility of free gas bubbles has been limited by their relative instability and inability to traverse the pulmonary and cardiac circulations. Solid particulate agents, though more stable, are less efficient acoustically and tend to be more toxic. Recently, experimental agents comprising sonicated human serum albumin and complex sugar molecules entrapping microbubbles of gas have been shown to survive the pulmonary and cardiac circulations and thus be suitable for peripheral venous injection. Using various animal models, including a natural hepatocellular carcinoma in the woodchuck, we have made both qualitative studies using imaging, duplex and colour Doppler, and quantitative studies from which the first small-vessel dose–response curves have been established. The considerable potential for the use of intravenously injected ultrasound contrast agents in radiological diagnosis will be discussed.

Radiation pressure gradients and acoustic streaming in ultrasound fields

H. C. Starritt and F. A. Duck
Department of Medical Physics, Royal United Hospital, Bath, Avon BA1 3NG, UK

Streaming has been shown to occur in water in the fields of both therapy and diagnostic ultrasound transducers due to absorption of the acoustic energy of the beam. This paper discusses the forces which cause streaming. Predicted values for the radiation pressure gradient resulting from absorption of a linear beam and a sawtooth beam, obtained using equations derived by Nyborg (1965), will be presented. Pressure gradients in tissue of the order of 6 kPa mm^{-1} may be experienced during an acoustic pulse in a lithotripsy field, when a sawtooth waveform is assumed. The maximum corresponding value in a diagnostic field is an order of magnitude lower. In water the predicted pressure gradient in the field of a sawtooth wave is approximately 10 times greater than in a linear field although the values are considerably lower than those obtained for tissue. Predicted values for amniotic fluid are similar to those of water. Experimental results obtained using a focused diagnostic 3.5 MHz transducer are presented. The effect on the stream of inserting an acoustically transparent membrane at different locations in the field is described, as a method of demonstrating the contribution to the stream of local forces at each position.

Reference

NYBORG, W. L., 1965. *Acoustic Streaming in Physical Acoustics Principles and Methods*, ed. by R. T. Beyer (Academic Press, New York).

Theoretical models for the luminescence of X-ray phosphor screens

G. E. Giakoumakis
Physics Department, University of Ioannina, P. O. Box 1186, 451 10 Ioannina, Greece

There exists in the literature a large number of experimental papers on X-ray phosphor screens. In order for all these experimental data to form a basis for further investigation, it is necessary to develop a theoretical model explaining the experimental data and permitting predictions on the expected properties of screens made of other materials. In this paper two different theoretical models are presented: a uniform screen model and a granular screen model. The first model is more suitable for compact screens such as those prepared by evaporation, while the second model is more suitable for granular screens such as those prepared by sedimentation. For both models analytical expressions are derived which permit the calculation of the screens efficiency as a function of their thickness and the X-ray beam characteristics. Comparisons are given between the two models and between theoretical results and experimental data for a number of phosphor materials, both old (ZnCdS:Ag, CsI:Na etc) and new (Gd_2O_2S:Tb, Y_2O_2S:Eu etc). Some of the experimental data concerning the new phosphor materials have never been previously reported, and the corresponding measurements were carried out especially for this study. Commenting generally on the agreement between theory and experiment, we point out that depending on the phosphor material, screen thickness and X-ray beam characteristics, the agreement is satisfactory to excellent.

Portable chest radiography on the intensive care unit: a comparison of computed and conventional radiography

P. E. Jennings, S. Padley and D. M. Hansell
Department of Radiology, Royal Brompton National Heart and Lung Hospital, Chelsea, London SW3 6HP, UK

Consistent high quality portable chest radiographs are difficult to obtain. Computed systems using photostimulable phosphor plates have several advantages. (1) The wide latitude of these systems insures that retakes due to underexposure or overexposure are rarely necessary and the images are of consistent quality. (2) Digitization of the image enables post-processing such as contrast adjustment and edge enhancement. (3) The improved sensitivity over film/screen combinations allows a lower patient radiation dose. The main disadvantage of computed systems is lower spatial resolution. One such system has been in clinical operation at the Royal Brompton Hospital for the last 6 months. We present the results of a prospective trial to compare the performance of computed with conventional radiographs in 50 post-operative patients. The images were assessed separately by three radiologists and the visibility of cardiovascular devices, in particular their course and tip, was scored on a five point scale of confidence. Computed radiography proved superior for the detection of prosthetic cardiac valves, mediastinal and intercostal tubes. Wilcoxon matched-pair tests confirmed a greater level of confidence in the identification of the courses and tips of devices on computed radiographs. The reasons for variation in levels of conspicuity between the different modalities will be discussed.

Colour flow computed tomography

K. A. Miles and *M. P. Hayball
*Departments of Radiology and Nuclear Medicine and *Medical Physics, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK*

Tissue perfusion can be readily calculated from dynamic computed tomography data using time–density curves derived from regions of interest over the tissue and aorta. This data processing technique was further developed to create a perfusion map for any given slice location. A single location dynamic sequence was performed with 10 data acquisitions in 45 seconds using a Somatom Plus computed tomography scanner (Siemens). After a reference measurement, 1.0 second data acquisitions were performed every 3 seconds with greater temporal spacing later in the sequence (maximum 6.5 seconds). The data were transferred to a personal computer with each image compressed to a 256 x 256 matrix. The maximum slope of the time–density curve for each pixel was determined. The ratio of the maximum slope and the peak enhancement observed within an aortic region of interest gave an absolute value of perfusion which was then displayed using a colour scale. The technique combines quantitative functional information with good anatomical resolution and its potential applications include the study of regional perfusion within tumours and demonstration of changes in intra-renal blood flow.

Three-dimensional imaging of soft tissues

J. E. Gardener, R. Richards, A. Tan, A. D. Linney, A. Gillams and W. R. Lees
Departments of Medical Physics and Radiology, University College and Middlesex Medical School, London, UK

Three-dimensional (3D) imaging and display techniques are rapidly becoming established in diagnostic and surgical planning applications relating to hard tissues, for example maxillofacial and pelvic surgery. For soft tissues where the boundaries are not so well defined as the bone–tissue interface, special techniques are required in image acquisition and display. We have developed a general purpose medical graphics workstation which has already been used in a wide range of hard tissue applications including surgical planning and prosthesis manufacture. We have now used this workstation to produce 3D displays from soft tissues. The system provides for "surgical" removal of sections of the 3D image data in addition to interactive rotation, thresholding and slicing. For displaying soft tissue images these facilities are very important for viewing organs which may be obscured by overlying structures. We have investigated different ways of displaying the image data and in many cases the images produced are quite new. The special 3D nature of the images is best seen in interactive operation, although videotape recording is also effective and will be used in the presentation. The clinical soft tissue studies have so far included bile ducts, oesophagus and rectum, intravascular ultrasound and obstetric ultrasound. The potential benefits deriving from these techniques include improving diagnosis, measurement, surgical planning and teaching.

Three-dimensional demonstration of biliary anatomy in obstructive jaundice

A. Gillams, W. Lees, *R. Richards, *A. C. Tan,
*J. Gardener and *A. Linney
Department of Radiology, The Middlesex Hospital and
**Department of Medical Physics, University College*
Hospital, London W1, UK

Three-dimensional (3D) computed tomography is well established as a means of defining complex bony anatomy both in craniofacial surgical planning and orthopaedic trauma. Our aim was to develop a technique by which 3D images of the biliary system could be generated. Contiguous 4 mm slices were obtained through the liver on a 256 x 256 matrix. 200 ml of intravenous contrast was injected dynamically, and scanning started after the first 100 ml. The 3D images were reconstructed on the MGI workstation using surface rendering techniques. Isolation of the bile ducts was achieved by selecting the appropriate threshold attenuation value. Superficial structures that might have obscured the view of the ducts were removed. The images were then viewed from multiple angles. Four patients (two male, two female) have been studied. In all cases there was excellent display of the biliary anatomy. Three patients had malignant obstruction at hilar, ampullary and mid-common bile duct (CBD) levels respectively. In the fourth, a pancreatic pseudocyst obstructed the distal CBD. The exact relationship of the CBD to the cyst was clearly demonstrated. We anticipate that in patients with hilar cholangiocarcinoma this technique will provide better appreciation of the segmental anatomy and of the volume of liver decompressed after interventional drainage procedures.

Semiautomatic quantitative evaluation of digitized skeletal radiographs

P. Gerhardt, W. Golder and A. Wunderlich
Intitut feur Roentgendiagnostik, Technische Universitaet
Muenchen, D-8000 Muenchen 80, FRG

Imaging plate digital radiography provides the unique opportunity to evaluate skeletal radiographs in a quantitative manner when using a specialized workstation. In this way, measurements of bones and joints can be improved, standardized, and made more popular for daily practice. The aim of this study was to develop software suitable for all-purpose quantitative evaluation of skeletal radiographs. The methods and results were as follows: critical evaluation of all usual roentgenometric procedures found in the radiological literature; selection of 70 appropriate parameters (distances, angles); definition of reference and abnormal values (according to age and sex); textural and graphic design of the material; design of the user's manual; connection between expert system and interactive workstation of the digital radiography system; practical evaluation of the programme. The new expert system will create a uniform scientific and technical basis for skeletal roentgenometry and hopefully enhance the quantitative evaluation of digitized radiographs in orthopaedics, traumatology, rheumatology, paediatric radiology, obstetrics and oromaxillary surgery.

Image quality in computed radiology

A. Workman and A. R. Cowen
Department of Medical Physics, The General Infirmary,
Leeds LS1 3EX, UK

Photostimulable phosphor computed radiography (PPCR) has been regarded as a digital imaging modality which could potentially replace the use of screen/film systems in many radiographic examinations. As part of the Department of Health FAXIL evaluation programme we have had the opportunity to assess the performance of PPCR in a wide range of radiographic examinations and to evaluate objectively the image quality of such a system. To aid this evaluation we have developed methods to derive objective image quality measures (such as modulation transfer function and Wiener spectra) from digital images. We have also applied similar measures to screen/film systems currently used in our X-ray department. For comparative purposes these results may be combined to produce absolute image quality measures such as the spatial frequency dependent noise equivalent quanta and detective quantum efficiency. Results are presented for PPCR and screen/film systems. Furthermore, the results of subjective quality evaluation using threshold contrast detectability tests are presented. We thank the UK Department of Health for support.

4.15 – 5.30

Teach-in: Update on Paediatric Gastric Studies

Balmoral Room

H. Carty and *D. Shaw
*Royal Liverpool Childrens Hospital, Alder Hey, Eaton Road, Liverpool L12 2AP and *Department of Radiology, The Hospital for Sick Children, Gread Ormond Street, London, UK.*

The Refresher Course will address the problems of the techniques of achieving gastro-intestinal studies of child, concentrating on common problems such as intussesception, gastroesophageal reflux, constipation and abdominal pain. The role of the old and new imaging techniques will be reviewed. We also propose to discuss when investigations should be instituted, and to cover practical hints in the difficult child.

Tuesday 30 April

9.00 – 10.15

Body MRI

Clarence Room

MRI of major mediastinal vessels

W. D. Foley
Radiology, Digital Imaging Section, Medical College of Wisconsin, Milwaukee, Wisconsin 53226, USA

Magnetic resonance imaging is a non-invasive technique for evaluating the thoracic aorta, pulmonary artery and superior vena cava in multiple imaging planes. Gated axial spin echo (black blood) is used in conjunction with gradient echo (bright blood) in a fast scan mode or retrospective cine mode review. Axial plane is complemented by parasagittal plane imaging. Major indications include suspected aortic dissection, aortic aneurysm, coarction, congenital heart disease, pulmonary artery anomaly and superior vena caval obstruction. Technique accuracy in imaging of aortic dissection is equivalent to dynamic contrast-enhanced CT. Magnetic resonance imaging is best utilized as an elective procedure rather than in the acute setting. In an elective setting, MRI is preferable to CT as contrast injection is not required and multiplanar imaging can be performed. Both MRI and CT are comparable in the evaluation of the thoracic aorta in post-operative patients. Magnetic resonance imaging artefacts secondary to phase effects can be recognized and compensated by re-orientation of the phase encoding gradients.

The contribution of magnetic resonance imaging in the assessment of suspected uterine enlargement

R. W. Kerslake and B. S. Worthington
Department of Radiology, University of Nottingham, Nottingham NG7 2RD, UK

The uterus is clearly depicted on T_2-weighted magnetic resonance (MR) images by virtue of its characteristic trilaminar zonal anatomy. This permits clear separation of extrinsic from intrinsic pathology, which, allied with the additional advantages of MR imaging (excellent soft tissue contrast, large field of view and lack of artefacts) results in excellent potential for accurate diagnosis. Pelvic MR imaging was performed at 0.15 T using a variety of pulse sequences in over 50 patients presenting with suspected uterine enlargement. The pathological diagnoses in those patients in whom uterine enlargement was confirmed included leiomyomas, leiomyosarcoma, other uterine sarcomas, cervical and endometrial tumours, pyometra and haematometra. Pelvic masses arising from other structures which masqueraded as uterine masses were also encountered and the appearances of these are contrasted and compared with those lesions of uterine origin. The strengths and limitations of MR imaging in the assessment of uterine enlargement are discussed with reference to appropriate examples and the optimal MR techniques are considered. Particular difficulties in the diagnosis of some endometrial pathologies are highlighted. It is concluded that there may be a useful ancillary role for MR imaging, especially when clinical examination and ultrasound are indeterminate.

Magnetic resonance guided biopsy

H. Baddeley, L. Caine and A. Shaw
Paul Strickland Scanner Centre, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, UK

Magnetic resonance (MR) imaging has an increasing role in oncological diagnosis, particularly in the demonstration of tumour recurrence following surgery, radiotherapy or chemotherapy. The discrimination between recurrent tumour and post-radiotherapy change can sometimes be difficult on imaging criteria alone. A needle designed specifically for MR guided biopsy is now available (Lufkin et al, 1987). The Lufkin needle is made of a steel alloy with low carbon and high nickel content, which is not attracted magnetically and which has no detrimental imaging artefacts although it is visible on the MR image. Magnetic resonance guided biopsy has been performed in a number of patients in whom the distinction between recurrent tumour and post-radiotherapy change could not be made confidently on imaging criteria. The results of MR guided biopsy in the patients examined and the technique for performing the examination will be described. The development of an alloy which may be used to manufacture instruments for MR guided interventional procedures obviously holds great promise.

Reference

LUFKIN, R., TENESI, L. L. & HANAFEE, W., 1987. New needle for MR guided aspiration cytology of the head and neck. *American Journal of Roentgeneology*, 149, 380–382.

Magnetic resonance imaging in the problem pelvis

J. Kabala and P. Goddard
Bristol Magnetic Resonance Imaging Centre, Frenchay Hospital, Bristol BS16 1LE, UK

Following major intervention for malignancy (radical radiotherapy and/or surgery) the pelvis may become difficult to assess clinically and with conventional imaging modalities. A study was set up to examine the accuracy of magnetic resonance imaging (MRI) for pelvic tumour recurrence in 26 patients in whom clinicopathological follow-up has been obtained. All had received radical radiotherapy. Two patients had lymphoma, the remainder had carcinomas originating at the following sites: cervix 16 (three had undergone hysterectomy), rectum four (all resected), bladder two (one cystectomy), vagina one, ovary one. Transverse T_2-weighted and proton density scans (TR 1800 ms, TE 100 and TE 30 ms), transverse or sagittal short tau inversion recovery (STIR) (TR 1500 ms, TI 100 ms) and coronal T_1-weighted (TR 500 ms, TE 26 ms) sequences were performed. The radiologist's original opinion on the presence or absence of recurrent tumour was compared with the subsequent outcome. Magnetic resonance imaging produced 11 true negatives, 11 true positives, two false positives and two false negatives, giving a sensitivity, specificity and accuracy of 85%. Useful signs for a positive diagnosis were bone involvement, bulky mass(es) and high signal intensity on the STIR sequence. This sign, however, also contributed to the false positives.

Pulse sequence selection in the evaluation of ovarian pathology

B. S. Worthington and R. W. Kerslake
Department of Radiology, University of Nottingham, Nottingham NG7 2RD, UK

In the evaluation of ovarian pathology, appropriate choice of pulse sequence is necessary to decide best whether a mass is benign or malignant, pronounce on its tissue composition and achieve optimal detection of metastatic deposits in cancer. From experience in over 200 patients with ovarian disease of known histology, certain recommendations can be advanced. No single pulse sequence is ever adequate to define fully the margins or characterize a mass lesion. T_1- and T_2-weighted spin–echo (SE) sequences provide an estimate of the protein content of cysts, and show tissue heterogeneity, particularly the presence of low signal solid components which favour malignancy. High signal components on both T_1- and T_2-weighted SE sequences which suppress on an appropriate short tau inversion recovery (STIR) sequence reflect either lipid in teratomas or chronic haemorrhage in endometriomas. Discrimination usually follows from consideration of the pattern of heterogeneity. Tumours with predominantly low signal on these sequences have a fibrous tissue content, *e.g.* the comas. Coronal inversion recovery can demonstrate omental metastases and ascitic fluid is well shown on the modulus variant. The STIR sequence highlights metastatic and recurrent cancer; the high signal from bowel contents which can cause difficulties is avoided when using heavily T_2-weighted sequences (TE 120–160 ms) and deposits down to 1 cm in size are readily identified.

Clinical applications of magnetic resonance imaging in children

A. R. Wright, D. Kinsella, A. Duncan and P. R. Goddard
Bristol Magnetic Resonance Imaging Centre, Frenchay Hospital, Bristol BS16 1LE, UK

Four hundred and fifty-eight patients under the age of 16 have had 515 magnetic resonance imaging (MRI) scans over a 3 year period in a clinical MRI unit using a medium field-strength system. The mean age of patients was 10.3 years, although patients as young as 18 days were examined. The majority (61%) of scans were of the head and spine. Peripheral joints accounted for 19%, and other body areas the remaining 20%. Thirty-nine per cent of examinations were performed for tumours, most commonly malignant brain tumours. Twenty-eight per cent of scans were for orthopaedic indications, typically osteochondritis, knee problems and back pain. Twenty-three per cent were carried out for assessment of congenital abnormalities, mainly spinal and cardiac. The role of MRI in the paediatric age group is discussed. Particular reference is made to anaesthesia and sedation, monitoring and reasons for inadequate studies.

Magnetic resonance imaging of cerebellopontine angle lesions: the role of gadolinium-DTPA

D. G. Hughes, J. M. Hawnaur, J. P. R. Jenkins and I. Isherwood
Department of Diagnostic Radiology, University of Manchester, Manchester M13 9PT, UK

Acoustic neuromas account for up to 80% of tumours in the cerebellopontine angle (CPA), and with gadolinium-DTPA small intrameatal lesions can be demonstrated. The remaining lesions comprise a wide range of pathologies, and the aim of the study was to assess the role of magnetic resonance imaging (MRI) in differentiating between these lesions, particularly with the use of gadolinium-DTPA. Forty-seven consecutive patients (aged 18–72) were reviewed having been referred over the last two years with either a strong clinical and electrophysiological evidence of an intrameatal or CPA lesion but negative or equivocal imaging including computed tomography (CT). Magnetic resonance imaging was performed on a superconducting magnet system (0.26 T) using a head coil. Spin echo (SE700–2000/40–80) and partial saturation recovery (PSR500/18) sequences were performed. Thirty-eight patients received gadolinium-DTPA (0.1 mmol per kg body weight). Of the 47 patients, 19 had acoustic neuromas, bilateral in three. The smallest lesion detected was 2 mm. All lesions showed intense homogeneous enhancement with gadolinium-DTPA. Nineteen other lesions were demonstrated comprising five meningiomas, three jugular foramen neurofibromas, two epidermoids, two basilar artery aneurysms, one cholesterol granuloma, one nasopharyngeal tumour with intracranial extension, and five intra-axial tumours originally thought to be extra-axial on clinical and CT findings. In nine patients, of whom seven received gadolinium-DTPA, no lesion was defined. The wide range in pathologies in the CPA can be differentiated in the majority using MRI with gadolinium-DTPA. These results will be discussed.

Congenital uterine anomalies: magnetic resonance imaging evaluation

B. M. Carrington, Hedvig Hricak, Regina Nuruddin, Eduardo Secaf, Russell Laros and Edward Hill
Department of Radiology, University of California at San Francisco, School of Medicine, San Francisco, CA 94143, USA

To evaluate magnetic resonance imaging (MRI) in the assessment of congenital uterine anomalies, 29 patients underwent prospective MRI using 1.5 T ($n=20$) or 0.35 T ($n=9$) MR machines. Spin echo sequences (TR500–2500/TE20–60) were obtained in orthogonal planes with a matrix size of 192 × 256, and a slice of thickness of 5 mm with a 20% gap. The features recorded were external fundal contour, intercornual distance, uterine signal intensity, endometrial/myometrial width and ratio, and the extent and signal intensity of any septum. All MR examinations were correlated with hysterosalpingography, laparoscopy, hysteros copy or laparotomy. The anomalies identified were uterine agenesis or hypoplasia ($n=7$), unicornuate ($n=5$), bicornuate ($n=10$), didelphys ($n=5$) and septate ($n=2$) uteri. Magnetic resonance imaging correctly classified the anomaly and typical MR features were discerned for each anomaly. It was of value in the following: (1) differentiation between obstructed uterine anomalies and adnexal masses; (2) identification of a sub-group of three patients whose uterine septae consisted of myometrium superiorly and fibrous tissue inferiorly; (3) effect on management decisions in 20% of patients by characterization of septal tissue (which altered the surgical approach), or identification of anomalies where pregnancy remained possible, thereby allowing conservative management. Coincidental gynaecological pathology was identified in 10 patients (endometriosis ($n=3$), leiomyoma ($n=4$), hydrosalpinx ($n=2$) and ovarian cyst ($n=1$).

Magnetic resonance imaging using the short inversion-time inversion recovery sequence in the pre-operative localization of parathyroid adenomas

A. R. Wright, P. R. Goddard, J. R. Farndon, S. Nicholson, D. Kinsella and E. R. Davies
Bristol Magnetic Resonance Imaging Centre, Frenchay Hospital, Bristol BS16 1LE, UK

The majority of studies using magnetic resonance imaging (MRI) to localize parathyroid adenomas have to date concentrated on T_1- and T_2-weighted spin–echo sequences using surface receiver coils, thin slices and high field-strength systems. We have tried to localize parathyroid tumours with a comparatively low resolution fat-suppression technique using short inversion-time inversion recovery (STIR) sequences in conjunction with relatively high resolution T_1-weighted sequences. Slices of 8–10 mm were employed without the use of surface coils. Prospective localization of parathyroid adenomas was attempted in 16 patients with clinical and biochemical evidence of hyperparathyroidism. All had MRI as described above. Most patients also had thallium–technetium subtraction scans and ultrasound. Correlation with the results of surgical exploration yielded a sensitivity of 71% and a specificity of 94% for MRI, 44% and 100% for thallium-technetium subtraction

($n=15$), and 46% and 85% for ultrasound ($n=13$). We present the clinical and radiological findings with emphasis on the false-negative and false-positive MRI cases. We believe the STIR sequence has considerable potential in the preoperative localization of parathyroid adenomas in patients with hyperparathyroidism.

The marrow in sickness and in health: a magnetic resonance imaging insight

S. Blease, P. Cook and P. Goddard
Bristol Magnetic Resonance Imaging Centre, Frenchay Hospital, Bristol BS16 1LE, UK

Until the development of magnetic resonance imaging (MRI) there has been no way of non-invasively assessing the response of bone marrow to the trials of life and disease. The very constituents of marrow which render it invisible to X-ray irradiation are ideal for optimum imaging by MR with its unique sensitivity to fat and water. The lack of streak artifact from cortical bone, multiplanar imaging and variable contrast resolution are other important factors which make MR an ideal imaging tool for bone marrow changes. For the first time, the changes in marrow composition with age can be clearly demonstrated, and these are discussed. In addition, normal ageing changes which are well known to the pathologist but which could cause an imaging pitfall are presented. Marrow is exquisitely sensitive to a wide range of insults including tumours, trauma, treatment, infection and vascular disorders. In many instances these changes occur before any bony change could be detected by conventional radiography. Magnetic resonance imaging thus has a wide range of potential applications in this field, and in particular it has thrown new light on the response to trauma, avascularity and radiotherapy. The typical changes in a wide range of conditions are presented and discussed.

Assessment of extra occular orbital pathology using magnetic resonance imaging

P. Goddard, S. Blease, A. Case, P. Cavanagh, M. Cobby and J. Waring
The Bristol Magnetic Resonance Imaging Centre, Frenchay Hospital, Bristol BS16 1LE, UK

Forty patients with extra occular orbital pathology were examined using magnetic resonance imaging. A Picker VISTA 2055 0.5 T magnetic resonance scanner was used. The benign space occupying lesions studied included thyroid eye disease, meningioma, AV malformation and neurofibromatosis. The malignant conditions included lymphoma, optic glioma, rhabdomyosarcoma, plasmacytoma and spread from carcinoma of the nasopharynx. Other conditions studied included optic neuritis and Lebers optic atrophy. Gadolinium DPTA (Magnevist) was used in a minority of cases but was found to be particularly helpful in showing the extent of spread of malignant disease intracranially. Gadolinium was also shown to be efficacious in distinguishing an optic meningioma from the optic nerve in one case. Magnetic resonance imaging is an extremely useful tool in demonstrating a wide variety of pathology in the orbit and does not involve the use of damaging irradiation.

9.00 – 10.15

Fractionation in Radical Radiotherapy

Balmoral Room

Accelerated fractionation

A. Horwich
Academic Unit, Department of Radiotherapy and Oncology, The Royal Marsden Hospital and Institute of Cancer Research, Downs Road, Sutton, Surrey SM2 5PT, UK

Accelerated radiotherapy is a strategy designed to overcome rapid tumour proliferation as a cause of treatment failure. To some extent this can be assessed by measuring cell kinetic parameters of tumours prior to treatment; however, accelerated repopulation may also occur as a consequence of the initial component of a course of radiotherapy and it is not possible to measure this in patients. There are three major strategies of accelerated fractionation: (1) short course intensive treatment; (2) moderate acceleration with early gap; (3) moderate acceleration with concomitant boost. All these strategies achieve their object by reducing the overall treatment time. It is not yet certain whether tumour control will be compromised by reduced fraction sizes or gaps in treatment, or reduced total dose. The predicted toxicity of accelerated fractionation is increased acute reactions and these have been confirmed in the intensive short course treatments such as continuous hyperfractionated accelerated radiotherapy (CHART) but not in the moderate acceleration strategies. An increase in late reactions would not be predicted if sufficient time is allowed between fractions to allow full sublethal damage repair. Reports of myelitis after CHART suggest that 6 hours may be an insufficient interfraction interval. The Royal Marsden Hospital has completed a pilot study of accelerated radiotherapy with early gap in bladder cancer and a trial is proposed of accelerated radiotherapy to a dose of 60.8 Gy in 32 fractions over 26 days compared with 64 Gy in 32 fractions over 6.5 weeks. This schedule, which employs 2 fractions per day, will fit into the standard working day and has sufficient flexibility to allow for machine service and other machine down time without compromising the overall treatment time.

Continuous hyperfractionated accelerated radiotherapy at Mount Vernon

M. I. Saunders, S. Dische, E. J. Grosch, D. C. Fermont, R. F. U. Ashford, E. J. Maher and A. R. Makepeace
Marie Curie Research Wing for Oncology, Mount Vernon Centre for Cancer Treatment, Northwood, Middlesex HA6 2RN, UK

From January 1985 to March 1990, 263 patients were treated with continuous hyperfractionated accelerated radiotherapy (CHART). Early reactions in the mucosae of the mouth and pharynx have been pronounced but all have healed, while those in the skin have been less severe than with conventional radiotherapy. An unexpected late morbidity was radiation myelitis in four patients, but in other tissues including the skin, mucosae, the connective tissues and the salivary glands, late changes appear reduced compared with those after conventional radiotherapy. In 92 patients with squamous cell carcinoma of the major sites in the head and neck region, a complete regression at the primary site and nodes was achieved in 90%. This can be compared with 62% in similar patients previously treated with curative intent at Mount Vernon between 1980 and 1985; the difference was maintained in follow-up ($p = 0.003$). Of 75 assessable patients with non-oat cell carcinoma of the bronchus, a complete radiological response has been achieved in 40% compared with 12% in a retrospective group; again the difference has been maintained in follow-up ($p = 0.0001$). With a reduction in permitted dose to the spinal cord, CHART gives promise for improvement in tumour control and a reduction in late morbidity. These promising results have led to multicentre randomized controlled clinical trials.

Parotid gland function following accelerated and conventionally fractionated radiotherapy

M. D. Leslie and S. Dische
Marie Curie Research Wing for Oncology, Mount Vernon Centre for Cancer Treatment, Northwood, Middlesex HA6 2RN, UK

Irradiation of salivary tissue during the treatment of head and neck cancer may lead to considerable dryness of mouth. Clinical experience with continuous hyperfractionated accelerated radiotherapy (CHART) has suggested that salivary gland impairment is less than that seen following conventionally fractionated radiotherapy. Parotid function has been studied in patients treated for head and neck malignancy using a unilateral technique that included one parotid, but spared the contralateral gland. A total of 26 patients have been studied, 18 with squamous cell carcinomas (six treated by CHART and 12 treated by conventionally fractionated radiotherapy to a dose of 60–66 Gy) and eight with lymphoma treated by conventionally fractionated radiotherapy to a dose of 35–40 Gy. Parotid function following radiotherapy was assessed by determining salivary flow rate and pH. The results demonstrate that following radiotherapy with CHART, there is significantly less reduction in parotid function when comparison is made with those given conventionally fractionated radiotherapy to a dose of 60–66 Gy.

Accelerated radiotherapy for carcinoma of the breast

V. H. J. Svoboda, J. Krawczyk and A. Krawczyk
Department of Radiotherapy and Oncology, St Mary's Hospital, Portsmouth PO3 6AD, UK

Accelerated radiotherapy is today being tested mainly in quickly proliferating tumours. We shall report on our 18 years experience with fast regimes in the treatment of 108 women with breast cancer; 15 of them received post-operative treatment, 18 were treated for local recurrence after primary radiotherapy, and the rest had radiotherapy for locally advanced tumour. The majority (87) was treated by three sessions a day with a minimal interval of 3 hours, 10 were treated twice a day, and the rest four times a day. Forty-nine patients received a course of treatment consisting of 15 fractions. The total overall time was only 5 days in 56 patients. The actuarial 5 year local tumour control was achieved in a quarter of patients with inoperable disease. The acute tolerance was very good. Late damage at 2 years occurred mainly in patients who were previously irradiated. The tolerance for different regimes will be documented by clinical slides and tables. Accelerated radiotherapy of breast carcinoma has limitations similar to those of daily fractionation but has logistic advantages and is very convenient as a palliative method. The slow proliferation of the tumour does not reduce its effectiveness.

Carcinoma of the thoracic oesophagus treated by radiotherapy: the Mount Vernon experience 1980 – 1989

M. D. Leslie, S. Dische, M. I. Saunders and B. E. Lyn
Marie Curie Research Wing for Oncology, Mount Vernon Centre for Cancer Treatment, Northwood, Middlesex HA6 2RN, UK

Between 1980 and 1989 a total of 244 cases of carcinoma of the thoracic oesophagus were referred to the Oncology Centre at the Mount Vernon Centre for Cancer Treatment. Those referred following surgery or tumour intubation and those referred for treatment of metastatic disease were not studied further. One hundred and forty received radiotherapy as the sole initial treatment of their primary tumour. Twenty-one patients were known to have metastases at the start of treatment and a further nine failed to complete their planned treatment due to deterioration in condition. The remaining 110 patients are the main subject of this study. The mean patient age was 72 years (range 48–94) and the female to male ratio was 1.2:1.0. The tumour site was upper thoracic in 19 (17.3%), mid in 54 (49.1%) and lower in 37 (33.6%). The mean tumour length determined from barium studies was 6.6 cm (range 2 – 14 cm). There were 104 (94.6%) squamous cell carcinomas, four (3.6%) adenocarcinomas and two (1.8%) anaplastic carcinomas. The median survival from the first day of treatment was 8.2 months (range 0.2 – 54 months). Improvement in dysphagia was achieved in 75 (77.3%) cases and the median duration of relief was 24 weeks (range 0 – 208 weeks). We conclude that radiotherapy has a valuable role in the palliation of this condition.

Combined external beam and high dose rate intracavitary radiotherapy for carcinoma of the nasopharynx: preliminary results

J. B. Wang, J. Y. Lang, H. Wen, F. Shu, X. Z. Zhang, J. L. Yang, W. Zhang and N. Y. Chen.
Department of Radiation Oncology, Sichuan Cancer Institute and Hospital, Chengdu, Sichuan Province, 610041, People's Republic of China

From January 1989 to August 1990, 39 Stage II–IV (M_0) patients with grade 2–3 squamous cell carcinoma of the nasopharynx were primarily treated with our new method of combined external beam and high dose rate intracavitary radiotherapy (ExRT + HDR-ICRT). The follow-up period was 6–18 months. The selectron-HDR technique is described which uses special arrangements of applicators and ^{60}Co pellets to conform the isodose curve distribution pattern to the natural shape of the nasopharyngeal cavity. This is intended to ensure optimal individualized treatment. We adopt a system of seven dose reference points, A–E and $0_{1,2}$, mostly bony marks on radiographs, to measure precisely the doses at different parts of the nasopharynx and the doses at neighbouring normal structures. Our protocol delivered a tumour dose ExRT 50 Gy/ 5 weeks for T1,2 cases or 56 Gy/5.5 weeks for T3,4 cases; and HDR–ICRT dose 24 Gy/4F/2 weeks for T1,2 cases or 18 Gy/3F/1.5 weeks for T3,4 cases, at the C point. The total dose (ExRT + HDR–ICRT) at the C point was 74 Gy. After HDR–ICRT the complete remission was 100%. The 1 year local control was 100%, and the 1 year NED survival was 78% (18/23). The acute reactions were easily tolerated and the incidences of major complications, *e.g.* xerostomia and trismus, were remarkably reduced. We consider that our preliminary results are very encouraging, and our HDR–ICRT method is more rational than those methods of intracavitary brachytherapy reported by other authors for treating carcinoma of the nasopharynx.

Notes

Magnetic resonance imaging in the diagnosis of radiation myelitis

H. Baddeley, P. Bekiaridis, S. Dische and M. I. Saunders
Paul Strickland Scanner Centre and Centre for Cancer Treatment, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, UK

Radiation myelitis is one of the most serious complications of radiation therapy. The diagnosis is usually made on clinical findings, and, in the past, diagnostic radiology has not played a significant role except to exclude other causes of myelopathy. Magnetic resonance imaging (MRI) is proving effective in the diagnosis of spinal cord disease and was therefore used to investigate six patients in whom a clinical diagnosis of radiation myelitis was made; symptoms developed between 5 and 25 months following radiotherapy. In five of the six patients there were distinct MRI changes in the cord in segments corresponding to those affected clinically. In patients with suspected radiation myelitis, MRI is the investigation of first choice because it can positively confirm the diagnosis and exclude conditions which may give a similar clinical picture.

9.00 – 10.15

The Therapeutic Uses of New Isotopes

Lancaster Room

^{131}I MIBG therapy in the treatment of neuroblastoma

C. A. Hoefnagel, J. de Kraker, P. A. Voûte and R. A. Valdés Olmos
Department of Nuclear Medicine and Werkgroep Kindertumoren, The Netherlands Cancer Institute, 1066 CX Amsterdam, The Netherlands

Iodine-131 Iodobenzylguanidine (^{131}I MIBG) is a radiolabelled guanethidine analogue, which has been used with varying success for diagnostic scintigraphy in a range of neural crest tumours, which exhibit an active uptake-1 mechanism at the cell membrane and cytoplasmatic storage in neurosecretory granules. The high sensitivity (81–96%) and specificity (95–100%) of this test in pheochromocytoma and neuroblastoma led to therapeutic use of the agent in these conditions. A good and selective concentration and a long retention in the tumour are the basis for MIBG treatment. At the Netherlands Cancer Institute, 80 patients have together received 243 therapeutic doses of ^{131}I MIBG, the majority for neuroblastoma. In addition ^{125}I MIBG was used in two patients. The procedure and clinical results are discussed. In a phase II study in 50 patients with progressive recurrent disease, seven complete remissions, 24 partial remissions, stable disease in 10 and progressive disease in eight were observed. One patient was lost to follow-up. The duration of remissions varied from 2 to 38 months. Most of these patients were only treated with MIBG after other treatment options had failed. In general, the treatment was well tolerated by children and the toxicity was mild, provided the bone marrow was not invaded by the disease. The best results were obtained in patients with voluminous soft tissue disease. The observed response in advanced neuroblastoma, the non-invasiveness of the procedure, and the high metabolic activity of untreated tumours have permitted us to use ^{131}I MIBG therapy in a new protocol in newly diagnosed patients instead of combination chemotherapy pre-operatively. The advantages of this approach are that the child's general condition is unaffected prior to surgery and that chemotherapy is reserved to treat minimal residual disease. Six patients with inoperable neuroblastoma (Stage III and IV) were treated with 7.4 GBq (200 mCi) ^{131}I MIBG initially and 3.7 GBq (100 mCi) doses thereafter and then submitted to surgery. Decrease of the volume of the primary tumour was noted in five out of six catecholamine excretion was decreased in all patients and in two the bone marrow aspiration changed from positive to negative. Five children could be operated on with tumour excision of more than 95%. We conclude that ^{131}I MIBG therapy has a place in the treatment of neuroblastoma; pre-operative *de novo* therapy with this agent is feasible and may have its impact on the further strategy and outcome in these patients.

The principles of radionuclide therapy

D. Ackery
Department of Nuclear Medicine, Southampton General Hospital, Southampton SO9 4XY, UK

The concept of treating cancer by local radionuclide irradiation is not new; radioiodine has been used for many years for the control of differentiated thyroid tumours. The extension of this principle of targeted radiotherapy to treat other forms of malignancy has been limited by the slow development of radiopharmaceuticals which are sufficiently concentrated in tumour tissue to deliver specific and adequate local absorbed radiation doses. For the effective killing of tumour cells by radiopharmaceutical delivered irradiation, several factors need to be considered for each case. These are discussed in relation to recent advances in radiopharmaceutical methods of treatment.

Prostatic carcinoma: strontium-89 therapy for metastatic bone pain

V. J. Lewington
Department of Nuclear Medicine, Southampton General Hospital, Southampton SO9 4XY, UK

Bone pain in advance prostatic carcinoma is difficult to control and the quality of life for those who have failed or escaped hormone control is often very poor. Targeted radionuclide therapy using strontium-89 provides effective pain relief for up to 80% of patients, of whom 20–25% become pain free. Treatment is well tolerated, with minimal toxicity even in heavily pretreated patients. The clinical and scientific background to strontium-89 therapy will be discussed with reference to the results of recent trials. The efficacy of strontium-89 therapy is compared with alternative palliative treatments to define the place of strontium-89 in the management of advanced prostatic carcinoma.

Radionuclide therapy for medullary thyroid cancer

S. E. M. Clarke
Department of Nuclear Medicine, Guy's Hospital, London SE1 9RT, UK

Medullary thyroid cancer (MTC) is an uncommon thyroid tumour. Twenty per cent of MTC are familial occurring as part of the MEN Syndromes, Types 2A and 2B. Most MTC tumours are slow growing and patients may survive many years despite widespread metastases. Many patients are, however, symptomatic as a result of tumour peptide secretion. Symptoms include flushing and diarrhoea. The main therapeutic option in patients with MTC is surgery and radical neck dissection for the primary tumour. ^{131}Iodine ablation of remnant thyroid tissue is the subject of some debate but is usually undertaken in patients with familial forms of the disease or in whom familial disease is suspected to prevent further tumour development at the sites of C cell hyperplasia. ^{131}Iodine meta-iodo-benzyl guanidine (MIBG), initially developed for use in patients with phaeochromcytoma, is only taken up into sites of primary and recurrent tumour in 30% of patients. The use of therapy doses of ^{131}I MIBG have been reported in a total of 14 patients with palliation reported in 12 patients, partial remission reported in seven patients and complete remission reported in one patient. Doses of up to 300 mCi (11 GBq) have been used and repeat treatments at 2–6 monthly intervals undertaken to maintain the therapeutic response. ^{99m}Tc V Dimercapto succinic acid (DMSA) is another radiopharmaceutical that has been used to image patients with MTC with sensitivities of 80–85% reported. Substitution with ^{186}Re a β-emitter has now been achieved. Early results with this new agent are presented.

Notes

9.00 – 10.15

Management and Audit in Radiology

Norfolk Room

Diagnostic imaging in primary health care

J.P. Owen
Department of Radiology, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 4LP, UK

General Practitioners' access to diagnostic imaging facilities varies from full, open and unrestricted access through partial access to total embargo. Their dissatisfaction with these arrangements is supported by a growing body of evidence which suggests that their use of imaging facilities may be clinically and financially justified. Forthcoming changes in Health Service funding could greatly strengthen their case. Radiologists and General Practitioners need to improve their mutual communications, trust and understanding.

Improving clinical management through diagnostic imaging

I. Russell
Health Services Research Unit, University of Aberdeen, UK

The late Professor Archie Cochrane proposed that the adoption of new diagnostic technologies should be conditional on objective evidence, preferably derived from randomized trials, that their use either alters the natural history of disease or otherwise benefits patients. Although this advice is sound in principle, there are many problems in applying it. First, the link between improved imaging and improved patient outcome is long and complex. Secondly, most diagnostic technologies cover a wide range of diseases. Thirdly, the benefits of improved imaging are often intangible or otherwise difficult to estimate. One way around these problems is to concentrate on a rigorous evaluation of the effect of diagnostic imaging on clinical management. Both before requesting a scan and after receiving the result, doctors are asked to specify both their differential diagnosis and their current management plan. Only scans that change that management plan are regarded as beneficial. This technique is particularly effective in the evaluation of established diagnostic technologies (where randomization may be regarded as unethical). Careful data collection, followed by multivariate statistical analysis, yields decision rules that discriminate effectively between scans that will benefit clinical management and those that will not.

Clinical audit in radiology departments using a casemix system

P. Hoffman
Guy's Hospital, St Thomas Street, London SE1 9RT, UK

The objectives are to see if the casemix management system (CMMS) can provide information useful for clinical audit in a service department such as radiology. Aspects of departmental policy are being looked at to see whether the data held in the CMMS can confirm that the policy is being adhered to. As an example, our policy is that pre-operative chest radiographs should not be requested routinely. The number of admissions for each of several surgical specialties is compared with the number of chest radiographs taken prior to surgery and the result expressed as a percentage. The percentage is found to vary between specialties and the possible reasons for the variation and the validity of the requests is explored.

Audit of out of hours computerized tomography scan usage in a city centre hospital

M. J. Weston and P. R Goddard
Department of Radiodiagnosis, Bristol Royal Infirmary, Bristol BS2 8HW, UK

Out of hours computerized tomography (CT) scans are the most expensive to perform and the most technically demanding. To assess the effectiveness of the out of hours service, a prospective study of the first 100 requests in 1990 was performed. Clinicians completed a special request form prior to the scan and the scan result and its effect on management were noted. There were an average of 15 requests per month. Eighty-three per cent of requests were for head scans, 10% for rapid sequence scans of the aorta, 3% for the spine and 4% for other regions. The mean age was 46 with a range of 3 to 88 years. Twenty-seven per cent of patients were given intravenous contrast medium and 14% required ventilation. Thirty-five per cent of the head scans were normal. Two scans could not be performed. One CT report was later found incorrect. The positive head scans mostly confirmed the clinical diagnosis and allowed institution of appropriate management. Six of the positive head scans and one of the aortic scans gave unexpected findings. The vast majority of the scans were acted upon during the same night as the scan. Out of hours CT scanning is a worthwhile procedure which enhances diagnostic understanding and therapeutic direction.

Audit in action: significant reduction in barium enema screening time with no loss of examination quality

D. Horton, A. M. Cook and A. D. Taylor
Department of Radiology, Hull Royal Infirmary, Hull HU3 2JZ, UK

The double contrast barium enema is an examination of high patient radiation exposure. The National Radiological Protection Board state that this exposure could and should be reduced. Barium enema screening times were being recorded as part of the departmental audit programme. A study was undertaken to establish whether the screening times could be significantly reduced. Two radiologists (AMC and DH) identified ways to reduce the screening times without affecting quality. These will be discussed. Data were collated on an ICL DRS M40 computer. In July, the month before changes were implemented, the average screening times were 2.6 minutes (AMC) and 3.2 minutes (DH). In September, the month after changes were implemented, the average time was 0.9 minutes for both. Statistically this was a highly significant reduction ($p<0.01$). The enemas were independently reviewed by a gastroradiologist (ADT) to assess diagnostic quality. Six examinations (out of 106) were of non-diagnostic value due to inability to exclude lesions within areas of extensive diverticular disease or due to residual faeces. Three were from July and three from September. There was no difference in diagnostic quality between the two months. We conclude that barium enema screening times and patient radiation exposure can be reduced without loss of examination quality.

Does the child need an advocate?

C. Gyll
32 Sudeley Street, Brighton BN2 1HE, UK

What are the needs of a child during X-ray examination? The concept of patient care is often limited to its physical aspects. Sufficient attention is not always paid to the child's emotional and psychological needs, which vary markedly during development. Reassurance and explanation are needed even for the very young, and must be adjusted to the level of understanding. Staff need to develop verbal and non-verbal communication skills. Knowing how fears alter with the development of imagination means problems can be anticipated and avoided. Development of memory includes the ability to anticipate and thus feel anxiety, which can overwhelm and become uncontrollable fear. Doctors are taught child psychiatry but not child psychology and development. The training of radiologists does not equip them to understand the thoughts and feelings of a child under stress. The memory of a bad first experience of the imaging department can endure, and will make subsequent examination almost impossible. Advocacy arrangements for the child in our imaging departments need to be addressed.

Notes

10.45 – 12.00

The Liver

Clarence Room

Liver imaging

A. L. Baert
Department of Radiology, Universitaire Ziekenhuizen, B 3000, Leuven, Belgium

During the last decade, the number of imaging modalities for the study of liver disease has been constantly growing: nuclear medicine, angiography, ultrasound CT and more recently MRI have become part of the diagnostic modalities available in most large hospitals. Ultrasound has been proven to be highly sensitive for detecting focal liver lesions, but will only rarely allow differential diagnosis. The value of CT in the detection of small lesions (1 cm or less) is hampered by technical factors such as the level of breathholding and slice thickness. CECT performed during the portal phase after superior mesenteric artery injection is however actually the most sensitive method for detection of metastatic liver disease. The detection rate of focal liver lesions at high field strength MRI is equal or superior to CT. The results can be improved by IV superparamagnetic ironoxide (ferrite) injection. An MRI differential diagnosis of liver tumours is mainly based on signal intensity but also on morphological features. Large comparative studies are however still needed to assess the value of MRI in this regard as compared with CECT. Ultrasound and MRI are particularly helpful in defining hepatic anatomy prior to surgery, because of the excellent visualization of the hepatic veins and the possibility of multiplanar imaging. $^{99}Tc^{m}$ labelled red blood cell studies are successful in differentiating haemangioma from other focal liver lesions. If surgical treatment of focal liver lesions is considered, angiography is still necessary for precise demonstration of arterial anatomy. On the contrary, intra-arterial injection of oily iodine contrasmedia (lipiodol) is not accurate in the detection of secondary tumours in patients with hepatocellular carcinoma, as it accumulates in cavernous haemangioma. Frequently, the combined intra-arterial administration of lipiodol and chemotherapeutic agents is tested in some centres but its efficiency remains to be proven. Ultrasound and CT are both well suited for the diagnosis of diffuse or focal hepatic steatosis or changes produced by hepatitis and cirrhosis. Haemochromatosis can be proven both by CT and MRI. Both haemochromatosis and steatosis are however best qualified by CT. The correct choice and appropriate use of these techniques should not only consider sensitivity and specificity but also cost, accessibility, invasiveness and last but not least therapeutic consequences.

Intra-operative ultrasound and liver surgery

G. Plant
Basingstoke Hospital, Basingstoke, Hampshire, UK

The treatment of liver tumours has always included surgery as an option and this has been increasing in importance owing to improvements in technology and techniques. One of the critical factors has been the development in the imaging capabilities both pre- and intra-operatively. The pre-operative detection of liver tumours, particularly multiple ones, has become more sophisticated as radiologists and surgeons realized that even the best of the conventional enhancement protocols produced a pick-up rate of up to 80%. Intra-operative Ultrasound (IOUS) with sterilizable transducers during laparotomy gave several advantages. It has a pick-up rate of approximately 95%, it allows precise identification of the anatomical position of lesions and their relationship with the critical intrahepatic vascular structures and allows precise control of biopsy, cannulation and drainage of deep intrahepatic lesions. Examples of the use of IOUS, techniques and equipment are discussed. The place of IOUS with regard to new diagnostic techniques such as computed arterial portography are addressed.

Gastric carcinoma: does intra-operative ultrasound affect the surgical management?

M. Bradley, M. Griffin, S. Cheung, A. Li and C. Metreweli
Chinese University of Hong Kong, Department of Radiodiagnosis and Organ Imaging, Department of Surgery, Prince of Wales Hospital, Shatin, New Territories, Hong Kong

The increased sensitivity of intra-operative ultrasound of the liver has been well documented in the evaluation of many abdominal neoplasms, but the aim of this study is to ascertain whether this information affected the surgical management over and above surgical palpation of the liver in patients with gastric carcinoma. In view of the fact that the mortality rate for a radical gastrectomy may approach 5%, it is obviously important to know about liver metastases. Thirty patients with gastric carcinoma underwent pre-operative and intra-operative ultrasonography of the liver. No malignant pre-operative lesions were seen, but as expected the intra-operative ultrasound was more sensitive (20 intra-operative, 10 pre-operative). The surgeon palpated multiple metastases in two patients which agreed with the intra-operative ultrasound, but these small lesions (3–5 mm) were not seen pre-operatively. Thus in these cases, the management was not affected by the intra-operative ultrasound. However, as regards the non-palpable lesions, two solitary metastases were demonstrated by intra-operative ultrasound and positive guided biopsy. Surgical management therefore changed in these two patients (6.6%) owing to the intra-operative ultrasound. Therefore, we propose that, if intra-operative ultrasound demonstrates surgically non-palpable metastases, the surgeon may opt for palliative gastrectomy, but it is of little benefit for multiple metastases as these are likely to be palpable.

Review of hepatic segmental anatomy

S. A. Worthy, E. A. O'Grady and P. C. Rowlands
Department of Radiology, Royal Liverpool Hospital, Liverpool L7 8XP, UK

The advances in segmental hepatic resection surgery for primary and secondary tumours and for trauma have made accurate localization of lesions necessary. It is important that the radiologist and surgeon are both absolutely clear on a common system of segmental anatomy. The Couinaud system of segmental localization is generally accepted by European hepatic surgeons. This system divides the liver into four segments, divided by the hepatic veins. There is a further transverse division which divides the liver into superior and inferior portions. These planes may be readily and reproducibly identified both radiologically and at surgery. Resection along these planes preserves venous and biliary drainage and blood supply. Examples of computed tomography, magnetic resonance imaging and ultrasound of the liver are presented and correlation with segmental anatomy is made.

Lipiodol computed tomography in patients with malignant liver tumours: is it worth the trouble?

A. Adam, P. Dawson and L. Banks
Department of Diagnostic Radiology, Hammersmith Hospital, Ducane Road, London W12 0HS, UK

In the last few years there has been a vogue, emanating initially from Korea and Japan, for the use of lipiodol embolization of the hepatic artery in an attempt to enhance the yield of computed tomography (CT) of the liver in patients with hepatic malignancy. Specific patterns of uptake have been described for different kinds of liver lesion and great claims have been made for its usefulness. We present our data on 21 patients with a variety of primary and metastatic liver tumours examined in this manner in whom all definitive diagnoses were confirmed histologically either by percutaneous needle biopsy or at subsequent surgery. In only one patient did the procedure reveal a previously undetected lesion and in no case did it affect clinical management. Interpretation was difficult in a number of cases and a false positive result was seen at the site of the liver biopsy. Another patient with a malignant phaeochromocytoma exhibited a pattern "characteristic" of haemangioma. Another patient developed acalculous cholecystitis as a complication. We concluded that lipiodol-enhanced CT is not risk free and does not usually affect the management of patients with hepatic malignancy.

The computed tomography central dot sign in bile duct dilatation: a non-specific finding

J. S. Beswick and D. F. Martin
Department of Radiology, Withington Hospital, University Hospital of South Manchester, Manchester M20 8LR, UK

The appearance, on dynamic contrast enhanced computed tomography (CT) of the liver, of intra-hepatic portal vein radicals apparently lying within and completely surrounded by dilated biliary radicals – the central dot sign – has been described as being characteristic of Caroli's disease. We have reviewed the post-contrast CT images of 29 patients with obstructive jaundice. Of these, five were not suitable for assessment (two portal vein thrombosis, three poor image quality). Of the 24 remaining (age range 25–89 years), the clinical and radiological causes of bile duct obstruction were metastatic disease (four), pancreatic carcinoma (seven), cholangiocarcinoma (seven), biliary calculi (two), Caroli's disease (one) and others (three). In 17, including the patient with Caroli's disease, the central dot sign was present, indicating that this feature is a non-specific finding which can be frequently anticipated in patients with intra-hepatic bile duct dilatation from any cause.

Dynamic computed tomography in the assessment of liver blood flow in normal and cirrhotic livers

K. A. Miles, *M. Hayball, +A. K. Dixon and
†C. A. Seymour
*Departments of Radiology, *Nuclear Medicine, +Medical Physics and Medicine, and †University Department of Radiology, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK*

Liver blood flow was assessed using single-location dynamic computed tomography (CT) sequence time–density curves (TDCs) constructed from the spleen, right lobe of liver and aorta. Normal liver TDCs are seen to continue to rise after the spleen TDC has reached its maximum owing to additional contrast arriving via the portal circulation. Hence both hepatic arterial and portal perfusion can be assessed. Normal patients and those with known hepatic cirrhosis were studied. A hepatic perfusion index (HPI) was derived from the maximum slope of the liver TDC before the peak of the spleen TDC g_a and the maximum slope of liver TDC after splenic peak g_p using the equation, $HPI = g_a/(g_a + g_p)$. Measurements of splenic and hepatic arterial perfusion were made from the spleen, liver and aortic TDCs. The HPI was increased in cirrhotic patients and correlated with liver flow indices from scintigraphy. The increase in HPI in cirrhosis was found to be due to reduced portal flow as well as increased arterial flow. Splenic perfusion (as opposed to total spleen blood flow) was also reduced in cirrhosis. Dynamic CT can provide quantitative functional information about liver blood flow which may be of value in the assessment of patients with hepatic cirrhosis.

Notes

10.45 – 12.00

Biological Treatment in Oncology

Balmoral Room

Biological therapies

P. Selby
Institute for Cancer Studies, St James's University Hospital, Leeds LS9 7TF, UK

The rapid growth in our knowledge of basic biology together with the applications of DNA recombinant technology now mean that we have the opportunity to re-explore biological therapy for cancer. The generation of large quantities of pure cytokines means that they can be evaluated in the clinic for their therapeutic benefits. Knowledge is sufficient to begin rationally to explore how they should best be used. Interferons, Interleukin-2, haemopoietic growth factors and tumour necrosis factors are already in use in the clinic. Interferon and Interleukin-2 have a definite activity against several cancers. Current data for renal cancer and Interleukin-2 will be presented and reveals a consistent response rate at 16% in 173 patients together with a suggestion, by comparative analysis, of prolongation of survival. The activity of Interferon has been known for some years against several cancers and its role as a maintenance biological therapy is currently being explored and will be described. Tumour necrosis factor is disappointing although recent increasing knowledge of its biology may allow its re-examination and haemopoietic growth factors will certainly be used in some aspects of clinical cancer care in the coming decade.

Labelling index as a predictor of repopulation in human tumours

N. J. McNally and G. D. Wilson
CRC Gray Laboratory, PO Box 100 Mount Vernon Hospital, Northwood, Middlesex HA6 2JR, UK

There is extensive clinical evidence that repopulation during fractionated radiotherapy can limit local tumour control. Accelerated fractionation could overcome this problem. However, it will be necessary to reduce the physical dose such that the biologically effective dose to tumours in which repopulation is not a problem may be too low. For this and for practical reasons, such tumours may continue to be better treated by conventional fractionation. It would be an advantage, therefore, to predict which tumours might benefit from accelerated fractionation. Probably the most appropriate pretreatment parameter that describes the capacity for accelerated repopulation is the potential doubling time T_{pot}. This is a function of the labelling index LI and duration of the S-phase T_s, and can be measured by flow cytometry of biopsies taken several hours after injection of bromodeoxyuridine (BUdR). However, it is not always possible to give a patient an injection of BUdR. In that case, the LI can be determined from *in vitro* labelling of biopsies with BUdR (or ^{3}H-thymidine). We have determined the ability of the LI to predict short or long T_{pot} in tumours of several sites following *in vivo* labelling with BUdR, and calculated the false positive and negative rates for predicting T_{pot} less than or greater than 5 days. In head and neck tumours, the LI alone is quite a good predictor of T_{pot}, but in cervix, lung and colorectal tumours it is not. We suggest that, in general, the LI will not be a good predictor of repopulation in individual tumours so that *in vivo* labelling with BUdR will be necessary. Current prospective trials will establish whether or not this is correct.

Combined ^{131}I metaIodobenzylguanidine and high-dose chemotherapy with bone marrow rescue and in poor prognosis neuroblastoma

R. Corbett, S. T. Meller and C. R. Pinkerton
Department of Paediatrics, Royal Marsden Hospital, Sutton, Surrey SM2 5PT, UK

^{131}I metaIodobenzylguanidine (mIBG) targets radiation into neuroectodermal tissue. Studies show that 20–48% of children with advanced neuroblastoma respond to ^{131}I mIBG when given alone after initial chemotherapy. High-dose chemotherapy (HDT) with ABMT rescue is routinely used as consolidation treatment in advanced neuroblastoma. This study is presently examining the efficacy and toxicity of combined ^{131}I mIBG therapy with HDT and ABMT rescue. Five children (four male, one female) with a median age of 7.5 years (range 4–11 years) were treated, three at relapse and two after initial chemotherapy. A single infusion of ^{131}I mIBG (median activity 11.1 GBq, range 7.0–11.1 GBq) was followed by HDT, and ABMT 15–32 days later. High-dose chemotherapy consisted of carboplatin and melphalan in four patients, and vincristine, etoposide, carboplatin and melphalan in one. One patient developed a septicaemia and died, and another failed to engraft; both had extensive bone marrow infiltration at the time of mIBG therapy. The combined therapy was well tolerated by the three other patients. Two children have relapsed, and two are alive 6 and 18 months after ABMI. In the absence of extensive bone marrow metastases, combined therapy is an acceptable form of consolidation treatment. The most appropriate radiolabel, optimal administered activity and interval between radiotherapy and ABMT rescue are discussed.

Arterial infusion of adriamycin for hepatoma: can the addition of lipiodol allow dose modification?

N. Raby, C. Kalayci, P. Johnson, N. Dobbs, G. Metivier, L. Summers, P. Harper and R. Williams
Department of Radiology and Liver Unit, Kings College Hospital, Denmark Hill, London SE5 9RS, UK

Treatment of hepatocellular carcinoma by direct infusion of cytotoxic agent into the hepatic artery has several potential benefits. The addition of lipiodol to the chemotherapeutic agent has been suggested as a means of targeting the tumour with the drug. Preferential retention of adriamycin within tumour tissue for a prolonged period of time has been demonstrated. It may, therefore, be possible to modify dose regimens since, if more cytotoxic is retained within tumour for a longer period of time, then, in theory, less drug will reach the system circulation and there will be less in the way of systemic side effects. This may allow an increase in the dose of drug administered or more frequent administration of the currently recommended dose. It has only recently been possible to measure plasma levels of adriamycin and its active metabolite adriamycinol and this has enabled us to test the above hypothesis. We have examined a group of 28 patients with hepatocellular carcinoma. Adriamycin was given intravenously in 12, into the hepatic artery in seven and into the hepatic artery in combination with lipiodol in nine. Free plasma levels of adriamycin were measured in all patients following drug administration. In addition, the subsequent effect on white blood cell, red blood cell and platelet counts were monitored. Our results show that whichever method of administration is chosen there is no difference in the systemic levels of adriamycin or in the subsequent effect on marrow suppression. The reasons and implications of these findings are discussed.

Transcatheter arterial cytotoxic infusion for hepatoma: is the addition of lipiodol beneficial?

N. Raby, C. Kalayci, P. Johnson, G. Metivier and R. Williams
Department of Radiology and the Liver Unit, Kings College Hospital, Denmark Hill, London SE5 9RS, UK

The requirement for delivery of cytotoxic agents directly into the hepatic artery for management of liver tumours has resulted in a role for radiologists in patient management since selective catheterization of the hepatic artery is an established radiological procedure. The technique of "targeting" cytotoxic agents by mixing them with lipiodol is widely reported from Japan to enhance response rates in patients with hepatoma. Adriamycin is one if the few agents to show any cytotoxic effect on these tumours when given systematically. The addition of lipiodol has at least three potential advantages: (1) selective targeting of drug to tumour; (2) retention of drug within tumour for several days; (3) possibly some degree of arterial embolization. The current study is one of the largest reported outside Japan. We studied 50 patients with inoperable hepatoma. Adriamycin was given intravenously in 31 patients and adriamycin/lipiodol via the hepatic artery in 19. Patients were matched for age, tumour size and stage. The response rate was 14% in both groups and the survival curves of the two groups showed no significant difference. These results and the possible reasons for the difference from the Japanese results are discussed.

The significance of continuous following of tumour markers CEA, TPA CA 125, and TATI during control of endometrial cancer

Z. Stanojević, N. Potic Zečević, M. Milutinović, S. Filipović and B. Filipović
Department of Gynaecological Oncology, Institute of Oncology and Radiotherapy, Niš, B. Taskovića 48, Yugoslavia

The tumour markers represent a group of heterogenous substances and together with other parameters are useful in therapy estimation and early discovery of recurrent disease or metastases. In this study the markers CEA, TPA, CA 125 and TATI were simultaneously measured in women with endometrial cancer. All the patients were treated with primary hysterectomy followed by irradiation. The markers were measured at intervals of 3 months over a period of 1.5 years. The first group included 52 patients with a normal local finding over the complete control period. Twelve patients in the second group had local recurrences or metastases after 8 months on average. The results for the first group of patients showed the same values for all the markers measured as those for the group of 50 healthy women. Significantly higher values of TPA, CA 125 and TATI, but not CEA, were found in the second group. The values of the markers either increased simultaneously with clinical detection of relapse or could be found 3 months before it. The results suggest continuous measuring of TPA, CA 125 and TATI as helpful diagnostic criteria of relapse endometrial cancer.

Balmoral Room

Serum TPA, CA 125 and TATI levels in post-operative residual endometrial cancer

N. Potić Zečević, M. Milutinović, Z. Stanojević,
B. Filipović and S. Radić
Department of Gynaecological Oncology, Institute of Oncology and Radiotherapy, Niš, B. Taskovića 48, Yugoslavia

The determination of tumour markers in oncological patients is a useful parameter in following up and prognosis of malignant diseases. The values of elevated levels of TPA, CA 125 and TATI are relatively specific in endometrial cancer. In this paper a group of 75 women with cancer of the endometrium was observed. The tumour markers were initially measured in all patients in the period between surgical treatment and the start of combined radiotherapy. The second determination was performed 3 months after irradiation. There were two groups of patients, those with a normal local post-operative finding (60 women) and those with a post-operative rest cancer, Stage III (FIGO) (15 women). The same markers were determined in 50 healthy women whose results served as a control. For the first group, no differences were found between the standard values of tumour markers and the values found in the control group. In the second group a significant elevation of all three markers was found. The results show that the elevated levels of the markers are a significant index of the presence of residual tumour tissue.

An effect of radiotherapy on tissue polypeptid antigen (TPA) and tumour associated trypsin inhibitor (TATI) levels on inoperable cervix cancer patients

M. Milutinović, Z. Stanojević, N. Potić-Zecević,
S. Filipović, B. Filipović and I. Tomić
Department of Gynaecological Oncology, Institute for Oncology, 18000 Niš, Yugoslavia

Elevated levels of tumour markers in blood indicate the presence of cancer cells (division and destruction), except for slight temporary increases occurring in some non-malignant conditions. The study includes the analysis of TPA and TATI levels in blood for 52 cervix uteri cancer patients stage II and III (FIGO). All patients are treated by radical combined radiotherapy. The tumour marker levels were measured before the therapy and 1–3 months after the therapy was completed. The group was without any progression of the disease. Before the therapy was started, TPA levels were elevated to a high percentage in all patients, demonstrating a statistical significance in relation to the levels in 50 healthy women in a control group. The difference in TATI levels had not been demonstrated to be statistically significant. After completion of therapy, the level of TPA decreases or returns to its normal values significantly in comparison with the levels for patients with unchanged or elevated levels. The change in TATI is again without statistical significance. Decrease or a return to normal values of TPA level is a good indicator of the effect of an applied treatment.

Early detection of relapse after complete remission following treatment for metastatic germ cell tumour of the testis

I. R. Brand, *A. Rathmell, B. M. Carey and *W. G. Jones
*Department of Radiology and *University Department of Radiotherapy, Cookridge Hospital, Regional Radiotherapy Centre, Leeds LS16 6QB, UK*

Over a 10 year period 29 patients (seven seminoma, 22 non-seminoma) were treated with chemotherapy and/or radiotherapy for metastatic germ cell tumours of the testis. All achieved complete remission initially but later relapsed. We have analysed the patterns of and time-course to recurrence together with the relative value of clinical and radiological follow-up. Our results demonstrate that routine estimation of serum tumour marker levels is the single most important follow-up procedure. This was true even in patients who were previously marker negative and was the first indication of relapse in 55% of the study group. Clinical examination and routine chest radiography were of little value in asymptomatic patients. Chest radiography was the first evidence of relapse in only two cases (7%). The optimal frequency of follow-up computed tomography scanning remains debatable but in our series was the first abnormal investigation in only seven patients (24%). It was of particular importance in patients who had residual radiological abnormality following initial therapy.

10.45 – 12.00

Diagnostic Imaging: Proffered Presentations

Lancaster Room

The thymus gland in children: ultrasound is the imaging method of choice

P. I. Ignotus and E. J. Adam
Department of Diagnostic Radiology, St George's Hospital, London SW17 09T, UK

The purpose was to assess the feasibility of the hitherto unreported technique of ultrasonic examination and measurement of the normal thymus gland in children aged 2–8 when it would not normally be seen on the chest radiograph. If the normal anatomy were visible, then ultrasound would be the natural first investigation for questionable superior mediastinal abnormalities in young children. Fifty children in the study age group were examined using a 7.5 MHz sector scanner. Parasternal sagittal scanning was used, angling the probe to visualize the substernal tissues. Longitudinal and anteroposterior measurements of both lobes were taken. In 47 children both lobes were successfully visualized and measured. In one, neither lobe was adequately visualized, and in two the right lobe was not well seen. The range of left lobe length was 1.79–4.1 cm, and the anteroposterior diameter was 0.78–2.47 cm. The right lobe length was 1.54–4.02 cm and the anteroposterior diameter was 0.81–2.35 cm. The gland showed a characteristic echo texture. Even when the thymus is not visible on a chest radiograph it is easily visualized and measurable using ultrasound. It is therefore recommended that ultrasound should be the first investigation for suspected superior mediastinal abnormalities in young children.

A comparison of abdominopelvic computed tomography with ultrasound

W. J. Shatwell, T. M. M. Meagher, C. H. Woodham and D. R. M. Lindsell
Radiology Department, John Radcliffe Hospital, Headington, Oxford OX3 9DU, UK

One hundred and forty-four patients having abdominopelvic computed tomography (CT) in an acute general hospital were assessed independently with ultrasound (US). All the US examinations were done over a 6 month period by a consultant with an interest in US. Only patients with lesions primarily affecting bone were excluded. Computed tomography and US agreed completely in 96 (67%) patients and in a further 27 (19%) the conclusion was the same with minor differences in details. There was major disparity in 21 (14%) patients. Of this group, 16 (11%) were inadequately or incorrectly assessed by US and five (3.4%) by CT. In experienced hands there is a high correlation between CT and US, almost irrespective of the referral criteria. Ultrasound should remain the first line of investigation in the assessment of the abdomen and pelvis.

Influence of experience on phlebographic diagnosis of deep venous thrombosis

T. Y. K. Chan, W. L. Wong and M. Lea Thomas
Department of Radiology, St Thomas' Hospital, London SE1 7EH, UK

Three radiologists, with experience at consultant, senior registrar and registrar levels respectively, independently reviewed 161 lower limb phlebograms on two separate occasions. Only two diagnoses were made: the presence or absence of recent thrombosis in the ilio-femoral, femoro-popliteal and calf segments. Intraobserver and interobserver variations of the observations are studied. K statistics was used, which effectively excludes agreement attributable to chance. There is satisfactory agreement ($K > 0.6$) between the two readings for all three observers in the three segments. McNemar bias is insignificant in all cases. This appears to suggest that the three observers, regardless of their level of experience, are consistent in their own individual interpretation of phlebographic deep venous thrombosis. The interobserver K was also satisfactory between the consultant and senior registrar for all three segments, though the McNemar bias was significant in the ilio-femoral and femoro-popliteal segments on both readings. The number of discrepancies, nevertheless, was small. McNemar bias analysis on the consultant–registrar pair yielded the same results but the K was unsatisfactory ($K = 0.51$) in the ilio-femoral segment. A review of the discrepancies showed that post-thrombotic changes, poor filling and streaming and bowel gas were the confusing features that led to the junior doctor's misinterpretations. This study suggests that some, but not extensive, training in interpretation of phlebograms is necessary. Intraobserver variation is not significant. Double reporting may improve diagnostic accuracy only where there is great difference in experience between the observers.

Light reflective rheography as a first line imaging method for lower limb deep venous thrombosis

I. Harris, *R. S. Diggory and G. T. Abbott
*Departments of Radiology and *Surgery, Royal Liverpool Hospital, Broadgreen and Arrowe Park Hospitals, Prescot Street, Liverpool L7 8XP, UK*

We present the results of a prospective study to determine whether light reflective rheography (LRR) is a sufficiently reliable method for detecting lower limb deep venous thrombosis (DVT). The results of LRR were compared with those of venography in a group of 123 participating patients, all of whom were referred with symptomatology suggestive of lower limb DVT. Bilateral venograms were requested on four of these patients. From a total of 127 examined limbs, 44 (34.6%) exhibited venographically proven DVT. The results of LRR on this DVT positive group comprised 42 (95.4%) abnormal and only two (4.6%) normal traces. However, both venograms relating to the latter two patients demonstrated presumed tiny fragments of deep calf vein thrombus only. Neither patient was subsequently anticoagulated. Forty-four rheograms of the 83 patients with thrombus-free venograms were normal, 39 (47%) thrombus-free patients showing abnormal rheograms. These results suggest that LRR is sensitive enough in detecting lower limb DVT to be used as a screening procedure prior to venography. In our study, 34% of all the venogram requests for DVT could have been obviated by LRR screening without any significant DVT being overlooked.

Silent deep venous thrombosis and unreliability of clinical diagnosis

T. Y. K. Chan and W. L. Wong
Department of Radiology, St Thomas' Hospital, London SE1 7EH, UK

Seventy patients with clinical features of deep venous thrombosis (DVT) or pulmonary embolism (PE) confirmed on scintigraphy underwent bilateral ascending phlebography performed with a standard technique. The radiographs were reviewed simultaneously by two radiologists who had no prior knowledge of the clinical information. Comparison was then made between the clinical and radiographic findings. Fifteen patients presented with PE and no clinical features of DVT. Of these, DVT was present bilaterally in three patients, unilaterally on the right in four, and on the left in two. No DVT was demonstrated in six patients. Of the nine patients with clinical signs of bilateral DVT, six were confirmed on phlebography, two had DVT on only the left side, and one had no radiographic DVT. Of the 18 patients showing right-sided clinical features, two had bilateral DVT, nine unilateral (seven on right, two on left), and seven had negative findings. Nineteen patients had left-sided DVT clinically. Seven of these were confirmed. However, six patients had bilateral thrombosis, one right-sided and five were negative on phlebography. There was incomplete clinical information (not stating side of symptom) in nine patients. Two of these had bilateral DVT, one on only the right, two on the left and four had no DVT demonstrated. Excluding the nine cases with incomplete clinical information, clinical diagnosis was correct in only 43%(26/61) of the cases. 33%(20/61) of DVT was missed and there was over-diagnosis (false positive) in 25%(15/61). These findings reflect the unreliability of clinical diagnosis. Phlebography should be performed to exclude silent DVT in the presence of PE. Blind anticoagulant treatment of unconfirmed DVT, especially where there is a risk of haemorrhagic complications, must be avoided.

Overlapping biliary endoprostheses – how to solve the problem of stent occlusion

A. Adam, J. Jackson, M. E. Roddie, N. Chetty and I. S. Benjamin
Department of Diagnostic Radiology and Surgery, Hammersmith Hospital, London W12 0HS, UK

During the last two years, 81 biliary endoprostheses have been inserted in 51 patients with occlusion of the biliary tree due to malignant disease. The endoprostheses used consisted of a mesh of stainless steel delivered over a 7 French catheter (Wallstent, Medinvent SA). When released across the malignant stricture the stents expanded to an internal diameter of 1 cm. None of the stents have become occluded due to ingrowth of tumour. Occlusion due to encrustation of bile has not been observed, probably because of the large lumen of the endoprostheses. However, during the follow-up period, four patients were readmitted to hospital with stent occlusion due to growth of tumour above or below the endoprostheses, one patient presenting twice with this complication. The diagnosis of stent occlusion was established by ultrasonography and percutaneous cholangiography. Following percutaneous biliary drainage, a second endoprosthesis was inserted to overlap the proximal or distal end of the original endoprosthesis and extend beyond the occluding mass. In one case a plastic endoprosthesis was inserted through a metallic stent. The procedures were successful in relieving the obstruction in all cases. Occlusion of metallic endoprostheses appears to be less common than that of conventional plastic stents and the management of this complication is simpler than percutaneous replacement of conventional stents.

Direct puncture venography (cavernography) in the assessment of subcutaneous cavernous haemangiomata

A. H. Troughton and R. M. Paxton
Department of Radiology, Derriford Hospital, Plymouth PL6 8DH, UK

The conventional assessment of subcutaneous cavernous haemangiomata is difficult. Because the blood flow is sluggish, venography rarely shows the full extent of the lesion or its draining vessels. Arteriography is even less useful because there is no direct arterial supply. Post-contrast computed tomography and magnetic resonance imaging show the extent of the lesion but not the feeding and draining vessels. We present a direct cavernography technique in five patients in whom conventional methods provided insufficient pre-operative information for the surgeon. The lesion is first assessed clinically. Cavernous haemangiomata present with a non-pulsatile swelling and there may be blue discolouration of the skin. Size can vary with posture. There is no demonstrable bruit or thrill. A narrow gauge venous cannula is introduced directly into the swelling and water-soluble contrast medium is slowly injected under fluoroscopy. Spot films are taken as the lesion fills. After the radiographs, any remaining contrast medium is withdrawn through the cannula which is then removed. Digital pressure is applied as for a normal venipuncture. In all patients, the anatomy of the lesion was well shown and no complications occurred. Direct cavernography is a useful and safe procedure in the assessment of cavernous haemangiomata.

Ultrasound and ultrasound-guided fine needle aspiration in cervical lymphadenopathy

A. Ahuja, R. M. Evans, S. Rhys Williams, C. Waldron, C. A. van Hasselt, W. King and L. McGuire
Departments of Radiodiagnosis, Otolaryngology, Head and Neck Surgery and Pathology, Prince of Wales Hospital, Shatin, Hong Kong

During a period of 1 year, 200 patients with cervical lymphadenopathy in whom a head and neck malignancy was clinically suspected underwent ultrasound examination and ultrasound-guided fine needle aspiration. This report will describe and evaluate our technique of ultrasound examination and fine needle aspiration, the ultrasonic criteria for malignancy in cervical lymph nodes, and the correlation of ultrasound appearances with the pathological diagnosis. The sensitivity of ultrasound in detecting lymph nodes in the cervical region, allied with the specificity of obtaining a histological diagnosis via a fine needle aspiration, directly influenced the management of patients in this series. The clinical implications and advantages of using ultrasound in the assessment and treatment planning in patients with head and neck malignancy are discussed.

Radiological differential diagnosis between developmental anomalies and bony destruction of the foramen ovale and the foramen spinosum in patients with nasopharyngeal carcinoma

*J. B. Wang, F. Z. He and Z. Z. Lei
*Department of Radiation Oncology, *Sichuan Cancer Institute and Hospital, Chengdu, Sichhan Province 610041 and The First Hospital, Chongqing Medical University, Chongqing, Sichuan Province 630042 The People's Republic of China*

We report five types of anatomical anomalies of the foramen ovale in addition to the standard type on the basis of reviewing 500 radiographs of the base of skull: (1) defective medial bony wall, 11.1%; L (2) fusion of the foramen ovale with the foramen spinosum, 3.4%; (3) wavy margin, 15.7%; (4) large, 2.7%; L (5) honeycomb 5.4%. We report six types of anatomical anomalies of the foramen spinosum in addition to the standard type: (1) large; (2) fusion of the foramen spinosum with the foramen ovale; (3) defective medial bony wall; (4) fusion of the foramen spinosum with the foramen ovale and with sphenopetrosa fissure; (5) two-hole; (6) short groove. A lack of knowledge of various developmental anomalies of the foramen ovale and the foramen spinosum will cause confusion in radiological diagnosis of bony destruction of the base of the skull at the region of these foramena on nasopharyngeal cancer patients, and will cause further confusion in correct clinical staging of nasopharyngeal cancer patients. We advocate that the only reliable radiological sign for the diagnosis of bony destruction of the foramen ovale or the foramen spinosum is the detection of brokenness, blurring or disappearance of the dense bony cortex shadow of the margin of the foramen ovale or the foramen spinosum.

X-linked deafness, stapes gushers and a distinctive defect of the inner ear

*P. D. Phelps, +W. Reardon, +M. Pembury, †S. Bellman and §L. Luxon
**Royal National Throat, Nose and Ear Hospital, Gray's Inn Road, London, UK, +Institute of Child Health, London, UK, †Hospital for Sick Children, Great Ormond Street, London, UK and §National Hospital for Neurology and Neurosurgery, London, UK*

The association of X-linked mixed deafness with stapes gusher has been recognized for 20 years, and imaging studies by polytomography have shown dilatation of the lateral end of the internal auditory meatus in some cases. We have made genetic linkage studies in seven pedigrees in whom deafness was inherited in an X-linked manner. All patients had a full range of audiometric and vestibular function tests. Thin section high resolution CT in two planes was used to assess the state of the middle and inner ears. We found a distinctive inner ear deformity in some of the deaf males characterized not only by a wide bulbous IAM but, more importantly, by deficient or absent bone between the lateral end of the IAM and the basal turn of cochlea. We believe that this results in a communication between the subarachnoid space in the IAM and the perilymph in the cochlea, leading to perilymphatic hydrops and a "gusher" if the stapes is disturbed. Moreover, some of the obligate female carriers seem to have a milder form of the same anomaly associated with slight hearing loss. Genetic studies on some of the deaf males with apparently normal inner ear anatomy suggest a different locus on the X chromosome and hence a different pathogenesis for the deafness.

The role of computed tomography in planning endoscopic paranasal sinus surgery

M. J. Warren, *H. Whittet, P. Anslow, *C. Milford and *A. P. Freeland
*Departments of Neuroradiology and *Ear, Nose and Throat Surgery, Radcliffe Infirmary, Oxford OX2 6HE, UK*

Traditional paranasal sinus surgery is being replaced by less destructive and more physiological endoscopic methods. For this to be successful, detailed information on anatomy and extent of disease is required for operative planning. This study was designed to compare the accuracy of nasal endoscopy and computed tomography (CT) in providing this information. All patients with suspected paranasal sinus disease referred to the Ear, Nose and Throat Department underwent clinical assessment, nasal endoscopy and CT as outpatients. A retrospective review of the CT examinations of the first 100 patients has been performed blind to the clinical details or endoscopic findings. The middle meatus lies below the middle turbinate and is a common drainage channel for the paranasal sinuses. Obstruction of the middle meatus may result in chronic sinusitis. Anatomical variants such as concha bullosa and paradoxically curved middle turbinates, which predispose towards middle meatus obstruction, were identified using both techniques. Middle meatus pathology can be assessed by endoscopy although visualization is sometimes limited. In addition to demonstrating middle meatus pathology, CT also enables examination of areas hidden to the endoscopist such as the ethmoid air cells and sphenoid sinus. Whilst there is some overlap of information, the two techniques are complementary. A joint radiological and surgical approach is recommended.

Osteoporosis and chemotherapy-induced early menopause

M. A. Ratcliffe, *D. M. Reid, S. A. Lanham and *A. A. Dawson
*Departments of Rheumatology and *Medicine, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB9 2ZB, UK*

Using a dual-energy X-ray absorptiometer (DXA) a study was initiated to measure the bone mineral density (Bmd) of women with chemotherapy-induced early menopause to determine those who most need prophylactic hormone replacement therapy (HRT). Fifty women, 24 post-menopausal, 16 for longer than 18 months, and 26 pre-menopausal were recruited. All had had steroids and gonadotoxic agents. Ninety-two fit aged-matched pre-menopausal women were selected as a control group. the bmd was measured in all between L2–L4, and at the trochanter, neck, and Ward's triangle of one hip. Other influences on the bmd were screened for in the post-treatment groups and results revealed no thyroid or renal dysfunction or positive family history. The bmd results from the control group were not significantly different at all four sites from the 26 pre-menopausal patients. However, the results from the 24 post-menopausal patients were significantly lower than the controls, the significance increasing with the selected 16. Fifteen of the 24 had bmds lower than expected for their age, with seven below the lower quartile. To conclude, the steroid doses from chemotherapy regimes have no effect on bmd and using DXA we are able to select those needing prophylactic HRT.

Contrast media reactions in patients with HIV disease

A. K. Banerjee and K. Tung
Department of Diagnostic Radiology, Westminster Hospital, London NW2 4NR, UK

Recent reports have suggested that patients with HIV disease may have a higher risk of drug-associated reactions. Little information exists with regard to reactions to intravenous contrast media in these patients. We have studied the nature and incidence of contrast reactions prospectively in 90 patients with known HIV disease. All HIV patients who required intravenous contrast media for any radiological procedure were included in the study. All patients were given iopamidol 300 (niopam). Any reactions, both immediate (within 5 minutes of injection) and delayed (within 24 hours) were recorded. The 90 patients in the study were male homosexuals with an age range of 22–64 years, mean 35.8 years. Eighty-three were given contrast for enhanced computed tomography scans of the brain, abdomen, pelvis or thorax, three for venography, two for IVPs and two for angiography. The volume of contrast ranged from 50 ml to 250 ml. Minor reactions including flushing (26), pins and needles (eight), ageusia (three), warm throat (two), dry mouth (one), and nausea (one) were noted in 28 (31%) of the patients. No major reactions were recorded, nor were there any delayed reactions. Our preliminary findings suggest that low osmolar contrast agents can be administered to patients with HIV disease without an increased incidence of side-effects.

Notes

10.45 – 12.00

Central Nervous System

Norfolk Room

A critical approach to selecting patients for magnetic resonance imaging of the nervous system

I. Moseley
Lysholm Department of Radiology, National Hospital for Neurology and Neurosurgery, London WC1N 3BG, UK

Magnetic resonance imaging (MRI), although technically still in its infancy, has become the prime imaging technique for many diseases of the nervous system. There are, however, some conditions in which it is not the ideal method; furthermore, until fast imaging becomes a clinical reality, selection of patients will continue to be necessary on grounds of both time and cost even when MRI is evidently desirable. Since in X-ray computed tomography (CT) we already possess a very powerful diagnostic tool, it is useful to identify situations in which MRI, CT or another imaging procedure is most likely to produce all the information required for diagnosis and management. This paper will review the commoner diseases of the visual pathways, brain, spinal cord and peripheral nerves, and attempt to indicate the potential contribution and limitations of imaging techniques, identifying clinical presentations or disease contexts in which MRI, CT or another imaging technique represents the preferred initial or accessory imaging pathway.

Temporal lobe epilepsy: magnetic resonance imaging appearances and pathological findings

C. S. Barker, *J. M. Oxbury, A. J. Molyneux and +C. B. T. Adams
*Departments of Neuroradiology, *Neurology and +Neurosurgery, Radcliffe Infirmary, Oxford OX2 6HE, UK*

Patients with medically intractable temporal lobe epilepsy may benefit considerably from temporal lobectomy if suitably selected. The majority of these patients have mesial temporal sclerosis; others have low grade gliomas. A small number have other structural lesions such as cavernous haemangiomas or cysts. Cranial computed tomography, although good at detecting neoplasms, has been poor in identifying mesial temporal sclerosis. A retrospective study was made of the magnetic resonance (MR) appearances on axial and coronal spin echo images in 19 patients who subsequently underwent temporal lobectomy. Six patients had indolent gliomas; one of these also had mesial temporal sclerosis. All showed focal increased signal on T2 weighted images. One patient with a cavernous haemangioma had a mixed signal lesion on MR. Twelve patients had mesial temporal sclerosis alone. Magnetic resonance abnormalities included mildly increased signal in the medial temporal lobe on T2 weighted images, local distortion or loss of differentiation of the grey/white matter, or local atrophy. One patient had a normal MR scan. Magnetic resonance has an important role in the assessment of patients with temporal lobe epilepsy.

An audit of magnetic resonance imaging in the diagnosis of multiple sclerosis

N. Akhtar, R. Uberoi, *A. Stanners, *M. R. Campbell and P. R. Goddard
*Departments of Radiology and *Neurology, Bristol Royal Infirmary, Marlborough Street, Bristol BS2 8HW, UK*

Magnetic resonance imaging (MRI) is a sensitive way of diagnosing multiple sclerosis (MS). This study looks at the impact of MRI on diagnosis of MS. A Picker 0.5 T Vista HP 2055 scanner was used. Twenty-five patients with definitive or probable MS presenting before the availability of MRI were reviewed and compared with 25 patients presenting after the availability of MRI. The number of lumbar punctures (LPs), computed tomograms (CTs) and admissions for diagnosis were compared. There was significant reduction in LPs, CTs and diagnostic admissions after the availability of MRI. Before the advent of MRI, 70% of patients had LP, 60% had CT and the average admission for diagnosis was 1.8 days. After the availability of MRI, 33% had LP, 20% had CT and the average admission was for 0.6 days. This study concludes that although MRI appears to be an expensive tool in the diagnosis of MS, its availability results in a decrease in other investigations and is very cost effective and less invasive for the patient.

Does cranial magnetic resonance support the statistical link between sinusitis and multiple sclerosis?

S. Blease, A. Troughton, P. Goddard, A. Stanners and R. Bodley
Bristol Magnetic Resonance Imaging Centre, Frenchay Hospital, Bristol BS16 1LE, UK

A long standing hypothesis for the development of multiple sclerosis has been the invasion of the central nervous system by commensal organisms during episodes of acute sinus inflammation. Two recent studies have retrospectively examined the G.P. records of groups of patients with multiple sclerosis and demonstrated a statistically significant link between episodes of acute sinusitis and the first attack of multiple sclerosis. Magnetic resonance (MR) is exquisitely sensitive to cranial inflammatory lesions, and is therefore the first imaging technique that can consistently demonstrate the co-existence of sinus inflammation and active plaques of demyelination. It is therefore an ideal tool to use in the search for radiological evidence to support the sinusitis/multiple sclerosis theory. The routine scan sequences used in this institution for all cranial investigation allows for evaluation of disease affecting all the paranasal sinuses. Three hundred cranial MR scans were retrospectively analysed in three groups of 100: group 1 consisted of MS positive scans; group 2 consisted of MS negative scans (normal); group 3 consisted of other intracranial pathology. The incidence of sinusitis in each group was noted, including an identification of which sinus was involved. The results were then matched for age and the time of year at which the scans were performed prior to statistical analysis. These analysed results are presented and discussed.

A longitudinal magnetic resonance imaging study of neurological manifestations of HIV infection in a cohort of HIV positive haemophiliac children

S. R. Smith, P. H. B. Bolton Maggs, G. H. Whitehouse, T. E. Smith and L. M. Ball
Magnetic Resonance Research Centre, University of Liverpool and Department of Haematology, Royal Liverpool Children's Hospital, Liverpool L69 3BX, UK

Several studies have identified neurological abnormalities by magnetic resonance imaging (MRI) in HIV infection. These features include cerebral atrophy and focal high signal intensity lesions. In order to evaluate the relationship between MR features and other indices of disease activity, a group (n=11) of HIV positive haemophiliac children (age 6–16 years) have been enrolled in a longitudinal study to relate serial MR findings in HIV infection to clinical, neurological and immunological parameters of disease activity. Brain MRI was performed in sagittal and axial oblique planes on a 1.5 T Signa system using T1, T2 and proton density weighted spin echo sequences. A matrix size of 128 x 256 produced a scanning time of 15 minutes. Magnetic resonance studies were repeated at intervals of 6 months. These studies were reported by two radiologists using a standardized proforma. Ten of the 11 children had abnormal MR scans at entry into the study: supratentorial and subtentorial cerebral atrophy, in varying degrees of severity, was present in six cases; three had varying degrees of cerebral atrophy as well as multiple focal lesions and one patient had focal lesions only. Serial scans showed progression of cerebral atrophy, or an increase in focal lesions in seven of the ten, MR remained stable in two, and one patient with severe atrophy died during the subsequent year. None of the children had any overt neurological symptoms or signs. There was no clear relationship between MR findings and other measures of disease activity (T4 lymphacyte counts, p24 antigen level, HIV-related symptoms or opportunistic infections).

Can we reduce eye lens dose during brain computed tomography in the UK?

L. J. Yeoman, A. Britten, L. Howarth and E. J. Adam
Department of Diagnostic Radiology, St George's Hospital, London SW17 0QT, UK

Computed tomography scanning of the head represents an increasing source of radiation dose to the lens of the eye. The aims of this study were (1) to document radiation dose differences when scanning through the eye compared with angling to avoid it, (2) to examine the difference in severity of posterior fossa artefacts produced by the two scanning planes, and (3) to document radiographic practice for head scanning at centres throughout the UK. Twenty patients requiring unenhanced and enhanced brain scans had an examination performed with each of the two beam angulations. Eye doses measured by a thermoluminescent dosemeter showed an 8-fold decrease in lens dose when the beam was angled to avoid the orbits. The majority of our sample of 54 hospitals do not routinely avoid the orbit. 67% scan parallel to the orbitomeatal line and 15% scan parallel to Reid's baseline. When posterior fossa pathology is suspected, a minority modify the standard technique to reduce lens dose. From our small sample we suggest that posterior fossa artefacts are not significantly reduced by scanning with the primary beam passing through the eye, and there is a large radiation dose saving to the lens if it is angled away from the eye.

Magnetic resonance imaging of normal white matter myelination patterns

A. G. Clifton, B. E. Kendall and D. P. E. Kingsley
Department of Neuroradiology, Hospital for Sick Children, Great Ormond Street, London WC1, UK

In infants and young children, structural abnormalities and diseases involving the white matter must be diagnosed against the changing appearances of normal myelination with age. In order to assess normal myelination patterns and assess the limits of these, 40 children with localized lesions which did not involve the supratentorial structures or cause hydrocephalus were analysed. All patients were scanned using high field magnetic resonance imaging at 1.5T using an axial multislice optimized band width double-echo stir sequence (TR/TI/TE=3000/148/23/83 ms). The intensity of the signal return from all parts of the hemisphere was compared with that of the splenium of the corpus callosum, and the grey matter. The majority of children showed the following pattern: peripheral white matter returned similar intensity to the splenium; central white matter and that adjacent to the body was of higher intensity and appeared to lie between 25 and 50% of the difference between that of the splenium and the grey matter. In addition, approximately 20% of patients had scattered pin point foci of high signal, and streaks of high signal in the deep white matter. The significance of these observations will be discussed.

Subjective computed tomography appearance of increased attenuation of an intracerebral artery does not always represent thrombosis

B. C. M. Macpherson and C. Santosh
Department of Neuroradiology, Institute of Neurological Sciences, Glasgow G51 4TF, UK

Recent papers have claimed that the computed tomography (CT) appearance of increased attenuation of intracerebral arteries is confirmatory evidence of the diagnosis and site of thrombosis, thus enabling local infusion of thrombolytic agent to be performed early in suitable patients. To test the validity of this "dense artery" sign, we have performed attenuation measurements (HUs) on scans of patients with a variety of pathological conditions, as well as normals. The HU range of normal basilar arteries (46 – 62, mean 55) overlapped with that of basilar thrombosis (45 – 58, mean 53). In normals, the HU range of the middle cerebral artery (MCA) was narrower (30 – 42, mean 35), and for adjacent brain 35 – 39 (mean 37); no artery was subjectively dense. Apparent prominence of MCA was seen in patients with atrophy, due to widening of the surrounding cerebrospinal fluid space, but HUs were normal. Where the MCA was subjectively dense, the difference in attenuation between artery and adjacent brain was abnormally wide (greater than or equal to 10 HU). In proven infarction, increased attenuation of the artery or decreased attenuation of brain was found: each factor alone in 25%, and in combination in 50%. The HU range of the MCA was 37 – 62 (mean 50), and of brain, 26 – 48 (mean 31). However, subjective arterial density was also found in other pathological processes, including oedema and infection, due solely to decreased brain attenuation. Thus, the subjective appearance of increased attenuation of the basilar artery is not diagnostic, whereas density of the MCA is significant, but not specific, and other causes of change in attenuation values in artery or adjacent brain should be excluded before diagnosing infarction.

Computerized tomography of the brain in the elderly — too much, too late?

M. S. Bernard and H. Adams
Department of Radiology, Llandough Hospital, Penarth CF6 1XX, UK

Elderly patients presenting with stroke as a result of embolic and thrombotic events are now more likely to receive anti-platelet drugs or full anticoagulation. Many more are undergoing computed tomography (CT) of the brain to avoid hazardous anticoagulation in intracranial haemorrhage. Clinical diagnosis is often difficult in the elderly and CT may identify other treatable disorders such as subdural haematoma. Incurable conditions such as intracranial neoplasms may be diagnosed which not only offers prognostic guidance but also avoids the wasteful use of rehabilitation facilities. A prospective study was conducted to assess the influence of CT of the brain on the subsequent management in elderly patients. One hundred CT scans of the brain were performed in 98 patients between the ages of 62 and 95 years (average 80 years) over a 12 month period. All the patients had been admitted to the Department of Geriatric Medicine with acute neurological signs and symptoms. Seventy-four patients presented with signs and symptoms of focal intracranial pathology, 22 with non-focal signs or symptoms and four were undergoing repeat examinations. Thirty-five examinations were normal. Sixty-one patients were suspected of having cerebral infarction or intracerebral haemorrhage, 23 of having a space occupying lesion and 14 of having a subdural haematoma. Of the patients with suspected cerebral infarction or haemorrhage, 29 had uncomplicated infarction (46%), four had haemorrhagic infarctions (6%), three had intracerebral haemorrhage (5%) and two had an intracerebral malignancy. Ten of the patients with a suspected space occupying lesion had cerebral infarcts (43%) and four had an intracranial malignancy (17%). In none of the patients with suspected subdural haematoma was the diagnosis confirmed. The influence of the CT examination on the clinical management was assessed by two radiologists and a geriatrician using a questionnaire completed at the time of examination and subsequent review of the clinical notes at 6 months. The results are presented more fully and the clinical situations where CT was most useful are discussed.

Intracranial osteochondromas: diagnosis by computed tomography with three-dimensional image reconstruction

P. Grech, H. Kazzaz and A. L. Hine
Department of Radiology, Central Middlesex Hospital, London NW10, UK

Osteochondromas are benign bone tumours which can usually be readily diagnosed by conventional radiography when located in typical sites such as in the appendicular skeleton. Intracranial osteochondromas may rarely occur, most often arising from the base of the skull. At this site the tumours may produce no, or non-specific, plain radiographic abnormalities; axial computed tomography (CT) scanning may suggest the diagnosis of osteochondroma but the distinguishing features of the tumours are difficult to appreciate. We present three cases of intracranial osteochondroma where CT with three-dimensional (3D) reconstruction showed the relationship of the tumour to the underlying bone and demonstrated the characteristic connecting stalk. Such imaging enables a diagnosis of osteochondroma to be made with increased confidence. We recommend CT with 3D reconstruction in the investigation of localized areas of intracranial calcification, especially when located near the skull base.

Notes

12.15 – 1.15

3M Mayneord Memorial Lecture

Oxford Room

New advances in cancer imaging and therapy with radiolabelled antibodies

D. M. Goldenberg
Center for Molecular Medicine and Immunology at the University of Medicine and Dentistry of New Jersey, Newark, NJ 07103, USA

Anticancer antibodies have been conjugated with gamma-emitting radionuclides for external cancer detection by imaging methods (radioimmunodetection, or RAID), or with beta-emitting or alpha-emitting radionuclides, drugs, or toxins for antibody-guided therapy. Each immunoconjugate, however, is beset with unique problems and prospects in addition to the overall current limitations of anticancer monoclonal antibodies (MAbs) as carriers of cytotoxic agents. The success of antibody accretion in tumours is dependent on such factors as the following: the nature, immunogenicity, and specificity of the MAb; availability, density, and location of the target antigen in the tumour; tumour vascularization and vascular permeability; pharmacokinetics of the MAb in the host. Since cancer imaging depends on the ratio of counts in the tumour to counts in adjacent tissues, and not on the absolute uptake of the radioactive antibody in the tumour, success can be achieved even when only small amounts of antibody are targeted. Using antibody fragments, rapid uptake in tumour and clearance from background, adjacent tissues can be accomplished, thus permitting the use of short-lived, low-energy radionuclides, such as ^{123}I and ^{99}Tc^{m}. Using a recently developed method of labelling antibody fragments directly with ^{99}Tc^{m}, we have been successful in imaging very small tumours (less than 0.5 cm) by planar and single-photon emission computed tomography imaging methods, even within 2 hours of injection of the radioactive antibody preparation. Because of the need to compensate for the low tumour uptake of MAbs used in therapy, first generation therapeutic immunoconjugates are more likely to be radioimmunoconjugates, since the energy of the isotope will kill cells in the vicinity of the targeting ("bystander effect"). Nevertheless, good therapeutic results have been achieved in patients with radiosensitive tumours, such as lymphoma, treated with ^{131}I-labelled antibodies.

Notes

2.30 - 3.45

Imaging in Trauma

Clarence Room

Radiological services at the Queen's Medical Centre, Nottingham, for the M1 air crash

B. J. Preston, N. S. McConachie, F. M. A. Wilson,
R. H. S. Gregson, T. Jaspan and J. M. Rowles
Department of Radiology, University Hospital, Nottingham NG2 2UH, UK

On Sunday 8th January 1989, A Boeing 737-400 aeroplane carrying 126 passengers and crew crashed into the embankment of the M1 motorway. Initially there were 87 survivors, 39 of whom were taken to the University Hospital of the Queen's Medical Centre, Nottingham. A team of 31 radiographers and four radiologists used all five X-ray rooms adjacent to the Accident and Emergency Department. Patients with head and spinal injuries were further assessed in the computed tomography (CT) suite by four radiographers and a neuroradiologist. In the initial 3 hours, 168 radiological examinations (343 films), five CT scans of the head, one CT scan of the thorax and two angiograms were performed. During the following 24 hours there were an additional 134 examinations (216 films), one CT scan of the thorax and four CT scans of the spine. Subsequently, many radiological investigations were performed for the assessment of known injuries. The injuries sustained will be detailed. The role of the radiologists could be categorized into the following: reporting, management of investigations, special investigations, planning ahead. Problems were encountered with the call-out system, patients deteriorating and lack of resuscitation equipment, patient flow, documentation, equipment and delay in diagnosis of injuries. As a result of our experiences, important lessons were learned and recommendations for improving the operational policy of the X-ray Department for dealing with a major incident could be made. These will be discussed and then enumerated.

Preparing a radiology department major accident plan

D. I. Boxer
Department of Radiology, Central Middlesex Hospital, London NW10 7NS and St Mary's Hospital, London W2 1NY, UK

In order for a hospital to cope adequately with mass casualties, it must have an efficient, well rehearsed major accident plan. It is usually advantageous for the radiology department to have its own supplementary plan. Radiologists are not often involved in the preparation of the hospital plan. It is unlikely that integration of the radiology department will improve unless this is remedied. Potential problem areas should be identified in advance and remedies incorporated. These include: receipt of the major incident alert; patient documentation; reporting system; staff call-in; required staffing levels; staff dispersal; patient supervision; patient flow; post-disaster alterations in work load. These problems are discussed and possible solutions are presented, based on the experiences of hospitals, both in the UK and abroad, which have had experience of disaster management. Once a major accident plan has been formulated an exercise should be performed to test it and to familiarize staff with its working.

A new computed tomography method for demonstrating the site of cerebrospinal fluid leakage

M. N. H. Lloyd, P. M. Kimber and E. H. Burrows
Department of Neuroradiology, Wessex Neurological Centre, Southampton General Hospital, Southampton SO9 4XY, UK

Accurate definition of the site of cerebrospinal fluid (CSF) leakage is essential for successful surgical management of post-traumatic CSF rhinorrhoea. Previous imaging methods, including conventional computed tomography (CT) have been disappointing. We use a dedicated high-resolution CT technique which uses fine slices in coronal and sagittal planes with a bone algorithm for data manipulation. The site of the responsible fracture between cranial cavity and sinus is well demonstrated and additional features of adjacent intracranial air bubbles or adjacent sinus soft-tissue mass are frequently shown. The technique is described and the results obtained in 20 patients are discussed.

An audit of computed tomography in blunt abdominal trauma

A. R. Padhani and A. K. Dixon
Department of Radiology, Addenbrooke's Hospital and University of Cambridge, Cambridge CB2 2QQ, UK

We have reviewed 122 patients referred for computed tomography (CT) following blunt abdominal trauma between 1982 and 1989. The quality of each examination (as judged on hard copy images) was graded (unacceptable, poor, satisfactory, good, excellent). The principal reasons for unsatisfactory (unacceptable or poor) images were noted. The number of out of hours referrals was assessed, along with the type of CT system used (dedicated body or neuroradiological). The referral rate slowly climbed over the 8 year period (26 in 1989). Image quality was unsatisfactory in 64 (52%) patients (unacceptable 17, poor 47). Image quality did not improve with time. The chief reasons for unsatisfactory images were inadequate enhancement (49 patients) and artefacts (44). Image quality was unsatisfactory in slightly larger proportions of studies performed out of hours (35/58, 60%) and on the neuroradiological system (33/48, 69%) although in neither case did the difference reach statistical significance. It is interesting that so many examinations were of inadequate quality. Occasionally this was due to the clinical condition of the patient; more often it reflected poor technique. Methods for improvement are discussed; in particular, there is no place for a "half-hearted" abdominal examination as an "add-on" to a cranial study.

The lateral neck radiograph for suspected impacted fish bones – is it indicated?

R. M. Evans, A. Ahuja, S. Rhys Williams and
C. A. van Hasselt
Department of Radiodiagnosis and Otolaryngology, Prince of Wales Hospital, Shatin, Hong Kong

The Cantonese have a fervent love of eating fish and seafood, the vast array of seafood restaurants in Hong Kong verifies this fact. Eating fish is not without hazards, however, and the Cantonese methods of preparation only add to the dangers. This study reviews the role of the lateral neck radiograph that is traditionally taken in every patient who attends an Accident and Emergency Department with a history suggestive of impacted fish bone. The radiographs of 100 cases of proven impacted fish bones were mixed with the radiographs of 100 normal cases. These were then reviewed, without access to the clinical findings, by two experienced radiologists independently. The presence of any radio-opaque foreign body, soft tissue abnormality or gas within the soft tissues was recorded and the results correlated with the clinical findings. A review of local seafood restaurants was undertaken in order to determine the most commonly eaten species of fish in Hong Kong which were then radiographed, the relevant findings are discussed. A review of the literature together with our findings leads us to question the value of obtaining a lateral radiograph of the neck in every patient with suspected impacted fish bone.

Three-dimensional imaging of tibial plateau fractures

J. N. P. Higgins, J. P. G. Padley and F. Starer
Department of Radiology, Westminster Hospital, Horseferry Road, London SW1, UK

Three-dimensional (3D) reconstruction of tibial plateau fractures from axial computerized tomographic (CT) scans can assist the clinician in assessment and in planning surgical management. These images can be generated from axial CT scans using computer software that is readily available on many CT scanners. We present the 3D images of a series of patients who have had tibial plateau fractures of widely varying severity. Comparison of the 3D images with conventional CT, including coronal and sagittal reconstructions, demonstrates their superiority in conveying the anatomical relationships of the bone fragments. The use of this technique should be considered in all cases of tibial plateau fractures.

The assessment of groin pain in athletes by peritoneography with computed tomography

S. Blease and R. Hackney
Department of Radiology, Princess Alexandra Hospital, Royal Air Force Wroughton, Swindon Wiltshire SN4 0QJ, UK

Intractable groin pain of obscure origin is a significant problem to athletes in track, field and contact sports. A large number (78) of sportsmen with groin pain have been studied by a technique pioneered in the 1970s by Scandinavian radiologists, called herniography. This involved the direct injection of water-soluble contrast media into the peritoneal cavity. Various projections are then used to study the lower anterior abdominal wall. In the above study, 53 out of 78 athletes had surgery with positive findings in each case. 81% of the operated group resumed full athletic activities. This technique has not caught on in British practice, but with the general increase in sporting activity in this country new methods to study the multivarious problems that beset sportsmen are of increasing importance. Our initial experience with the technique of herniography (more correctly called peritoneography) is presented, and some modifications to the technique are described. These include post-exercise views and computed tomography scanning which has not been reported elsewhere in the literature. The relevant anatomy is reviewed and surgical correlation and results are presented.

Magnetic resonance imaging in the pre-operative assessment of urethral trauma

B. M. Carrington, H. Hricak, C. Dixon and J. McAninch
Department of Radiology, University of California at San Francisco School of Medicine, San Francisco, CA 94143, USA

Fifteen patients with post-traumatic strictures of the membranous urethra underwent prospective magnetic resonance (MR) imaging prior to open urethroplasty. Examinations were performed on a 1.5 T unit and patients had multisection spin echo sequences (TR 500–2500 and TE 20–70) performed in all orthogonal planes, with a matrix size of 192 x 256 and a 4 mm slice thickness with a 20% gap. Conventional retrograde and cystourethrography were also performed prospectively and independently. Compared with contrast urethrography, MR defined the length and location of urethral injury but provided additional information about the direction and degree of prostatic and urethral dislocation. On MR, perivesical and periurethral fibrosis were easily identified, together with any prostatic hypertrophy. The above features influenced surgical planning. Additional injuries identified on MR included fracture or dislocation of the corpora cavernosa and presacral fluid and/or fibrosis suggesting sacral nerve trauma. Both findings indicated a high probability of impotence. Ischial fractures were more readily seen on MR.

Notes

2.30 – 3.45

Low or High Dose Rate in Brachytherapy?

Balmoral Room

Low or high dose-rate in brachytherapy? The clinician's choice

R. Stout
Department of Radiotherapy and Oncology, Christie Hospital & Holt Radium Institute, Withington, Manchester M20 9BX, UK

The use of brachytherapy (interstitial, intracavitary and surface mould treatments) declined between 1950 and 1980, coincident with the development of megavoltage teletherapy equipment and an increasing concern to reduce the exposure of staff to ionizing radiation. Although manual low dose-rate and remote high dose-rate afterloading systems were developed in the 1960s, brachytherapy was increasingly limited to the treatment of uterine carcinoma and tumours of the anterior two-thirds of the tongue. Since 1980 there has been a resurgence of interest in brachytherapy following the advances made in remote afterloading technology. The problems of staff protection have been overcome and a range of consistently reliable treatment machines allow the radiotherapist to choose low, medium or high dose-rates according to personal preference, using conventional or miniature sources. The delivery of brachytherapy has been facilitated and extended to include organs previously beyond the practical scope of intracavitary or interstitial implantation. Spoilt for choice, and assuming that equivalent results with the same morbidity can be obtained using high dose-rate, what factors will influence the equipping of an average-sized department to provide a comprehensive brachytherapy service into the 21st century?

Low or high dose rate in brachytherapy?

I. Turesson
Department of Oncology, Sahlgrenska sjukhuset, 413 45 Gothenburg, Sweden

The use of interstitial and intracavitary radiotherapy, and also total body irradiation, requires more insight into biological differences between continuous low dose-rate and fractionated high dose-rate irradiation. It is well recognized that continuous low dose-rate irradiation applied by interstitial and intracavitary techniques results in a high local tumour control rate. With the advent of afterloading equipment for high dose-rate irradiation, the dose distributions are comparable for both modalities. From the biological point of view, the question is whether fractionated high dose-rate radiotherapy, often more attractive for logistical reasons, is a good alternative to the use of radium in the treatment of cervical and endometrial tumours, iridium implants for boosts to head and neck and breast tumours, and low dose-rate total body irradiation, to mention a few examples. The purpose of this paper is to focus attention on the dose-rate and fractionation sensitivity for various normal tissues. A scaling between dose rate and fraction size is presented. The arguments and the analysis are based on data from the literature on dose-rate effects, mainly on normal tissues, and experimental studies comparing the effects of continuous low dose-rate and fractionated high dose-rate irradiation.

Changing low dose rate brachytherapy into high dose rate brachytherapy: how many equivalent factors are necessary?

R. Schulz-Wendtland, M. Bauer and R. Richard
Department of Gynaecological Radiology, Radiological Centre of the University of Freiburg, 7800 Freiburg, FRG

The steep decrease in dose and dose rates in brachytherapy implies very different radiobiological considerations of the biological effectivity. Therefore, in imitation of the clinical procedure, we compared low dose rate (LDR) and high dose rate (HDR) brachytherapy. We carried out experiments on epidermoidal cervix carcinoma cells (Ca Ski-cells) and human primary keratinocytes obtained after transfection with human papillomavirus type 16 DNA, varying the dose rate (27–8000 cGy/h), the dose (1 – 100 Gy) and fractioning (protracted, 3, 6, 12 and 18 fractions). Our conclusions are as follows. When changing an LDR into an HDR brachytherapy, the equivalent factors close to the source have to be selected low, and as the distances from the source increase, they should become higher. The reduction of the dose in HDR radiation therapy is a compromise designed to limit side effects caused by radiation. The trade-off is a small therapeutic range and reduced therapeutic effectiveness at the tumour. Each increase in the dose rate requires higher fractionation but it may not be possible to replace LDR radiation by HDR radiation with high fractionation because tumour cells and healthy cells show different reactions. The percutaneous dose at the pelvis wall has to be reduced, if HDR brachytherapy is carried out at the same time, to avoid side effects.

Comparison of intracavitary insertions using isoeffect surfaces

C. Deehan and J. A. O'Donoghue
Beatson Oncology Centre and West of Scotland Health Boards, Department of Clinical Physics and Bioengineering, Glasgow, UK

The position of surfaces of equal biological effect (isoeffect surfaces) around an intracavitary insertion can be calculated using the linear quadratic (LQ) model. Isoeffect surfaces can be defined for different biological effects (*e.g.* acute effects and late effects). For a particular low dose rate (LDR) insertion some isoeffect surfaces will coincide, but when the dose rate is increased to the medium dose rate (MDR) or high dose rate (HDR) range they will dissociate. When replacing a single LDR insertion by a single MDR or HDR insertion, the dissociation distance is approximately 5–8 mm at point A. The dissociation distance can be reduced, eliminated or even reversed if the treatment is fractionated instead of given as a single fraction. The concept of isoeffect surfaces may be used to compare continuous intracavitary treatments of different dose rates. This approach can also be used if treatments contain both continuous irradiation and fractionated external beam radiotherapy.

Notes

2.30 – 3.45

Teach-in: Radiology in the Management of Lymphoma; the Oxford Joint Lymphoma Clinic

Lancaster Room

S. J. Golding
Department of Radiology, University of Oxford, UK

The lymphomas offer particular challenges to radiology because this is a rapidly developing subject in which the principles of investigation and management are changing under the impact of research and new developments. Effective treatment, either radical radiotherapy or chemotherapy, is available for the majority of patients and radiology is an indispensable component of many patients' management, but it must be closely related to the needs of the patient and the objectives of the clinician if it is to provide a reliable basis for treatment decisions. Rapid diagnosis is mandatory but primary disease is clinically evident in only a number of patients and extensive investigation is frequently required. Early recourse to accurate studies such as ultrasound and computed tomography (CT) may prevent delay in diagnosing deep-seated disease in chest and abdomen. However, the lymphomas may arise in a wide range of organs and may mimic other disease of those organs, so that organ-specific examinations may also need to be considered at an early stage. Treatment requires not only localization of disease but characterization of cell type and degree of cellular activity; conventionally this has required surgical biopsy of accessible disease or percutaneous biopsy of sufficient size to provide material for histology. However, this approach is now challenged by cytological techniques which yield information hitherto unavailable from aspiration specimens. Accurate disease staging is necessary in the majority of patients and relies heavily on radiological technique. Traditionally CT is the basis of staging but magnetic resonance imaging (MRI) offers certain advantages, especially in the investigation of bone marrow, where it may be an alternative to marrow biopsy. During treatment follow-up studies may be limited to areas of known disease, depending on the mode of treatment. A major problem in monitoring these patients is the residue remaining after treatment of a localized mass, which may represent active disease or fibrosis. Magnetic resonance imaging and high-dose Gallium scintigraphy may be of help in this situation, although percutaneous biopsy appears at present to be more reliable. Screening patients for recurrent disease is a controversial area and close liaison with the clinician is required to prevent unjustifiable investigation. As in other diseases, the radiologist has a responsibility to limit radiation dose to these patients, who are frequently young and may not undergo radiotherapy for treatment, but in whom there is a definite incidence of second malignancy. In this Teach-in, members of the multidisciplinary Oxford Joint Lymphoma Clinic approach how these factors influence their approach to the management of this disease.

Notes

2.30 – 3.45

Nuclear Medicine: General Session

Norfolk Room

New instrumentation in clinical nuclear medicine

P. J. Ell
UCMSM, UCL, London, UK

The Anger gamma camera has been with us since the early 60s, when Anger developed a radiation detector which would find medical applications for over three decades. Probably 90% or more of all the clinical work undertaken by nuclear medicine departments is carried out on such a device. The 70s have seen the advent of single photon emission computed tomography (SPET) and the 80s the widespread clinical applications of SPET. The 90s will see the spread of multiple detector technology for clinical SPET. It is the aim of this presentation to review present experience of multidetector SPET technology, its implications and potential for the practice of clinical nuclear medicine. Data is presented from a single slice multidetector brain scanner (the SME 810), from a dedicated three detector Anger gamma camera instrument for brain scanning (the IGE Neurocam) and from a dedicated three detector Anger gamma camera apparatus for brain and body tomography (the Toshiba GCA 9300/A). These instruments have been already used in the study of several hundreds of patients. It is clear that multiple detector technology for SPET represents the next step in a continuing process of improvement of nuclear medicine instrumentation.

Computer assisted interpretation of single-photon emission computerized tomography scans of the brain: a multimodal approach

E. D. Lehmann, D. J. Hawkes, D. L. G. Hill, C. F. Bird, G. P. Robinson and M. N. Maisey
Division of Radiological Sciences, United Medical and Dental Schools, Guy's Hospital, London SE1 9RT, UK

Single-photon emission computerized tomography (SPECT) and magnetic resonance imaging (MRI) brain scans from the same patient are aligned and scaled. This is done using four markers visible in both modalities. When patient MRI scans are not available an atlas derived from a segmented and labelled reference MRI data set is used. Patient SPECT scans are registered, in three dimensions, with this atlas using the same four markers and the location of the skull vertex. Once registered, corresponding two-dimensional slices from the two three-dimensional data sets can be displayed side by side on a computer screen. A cursor linking the two images allows the delineation of regions of interest in the SPECT scan based on anatomical structures identified either from the patient's MRI data set or the atlas. Clinical evaluation of this work has shown that aligned MR images can aid in the delineation of anatomical structures in functional SPECT scans of the brain. Furthermore, using a reference MRI data set could, in certain circumstances, obviate the need for a concurrent MRI investigation and therefore could be used by those centres which have SPECT but do not have access to MRI. Work is currently in progress to assess the accuracy of the registration techniques used and the validity of basing a neuroanatomical atlas on the MRI data set of a single individual. Preliminary measurements of the positions of structures in normal MRI scans which have been registered with the atlas have shown an overall r.m.s. displacement from the atlas of 7.8 mm. While these are only preliminary results based on a small number of patients, they do compare favourably with the 12 mm spatial resolution of the gamma camera used to acquire the patient SPECT studies.

Cranial computed tomography and single-photon emission tomography in Alzheimer's disease

C. S. Barker, J. Lawrence, *K. A. Jobst and +A. D. Smith
*Departments of Radiology and *Neurology and the +University of Oxford Department of Pharmacology, Radcliffe Infirmary, Oxford OX2 6HE, UK*

A prospective study of adults with varying degrees of mental deterioration and memory loss is in progress in Oxford. Computed tomography (CT) and single-photon emission tomography (SPET) scanning are performed on all patients. Axial CT parallel to the orbitomeatal line is followed by 4 mm sections of the temporal lobes parallel to their axis. In addition to a qualitative assessment of any pathological features, a specific measure of the medial temporal lobe widths is made. Single-photon emission tomography is performed using a bolus injection of 500 MBq of ^{99}Tc^{m} hexamethylpropyleneamine. Fifty-one of the 79 patients have a clinical diagnosis of Alzheimer's disease. Of those with clinical Alzheimer's, 49 have significant medial temporal lobe atrophy on CT and of these 44 have reduced perfusion in the parietotemporal region on SPET. Twelve patients have died; 10 had an histopathological diagnosis of

Alzheimer's disease. All 10 had the combined CT and SPET features described above. The reduced perfusion in the parietotemporal cortex may be related to loss of projection neurones in the parahippocampal gyrus that innervate this part of the cortex.

Evaluation of 11C-methionine uptake in breast cancer metastases using positron emission tomography

R. Huovinen, S. Leskinen-Kallio, K. Någren, M. Teräs, U. Ruotsalainen, E. Nordman and U. Wegelius
Turku Medical Cyclotron-PET Center, Turku University Central Hospital, 20520 Turku, Finland

Positron emission tomography (PET) with use of adequate radiotracers is an excellent method in oncology for detecting tumours, monitoring therapy and studying tumour biology *in vivo*. The use of 11C-methionine (11C-met) is based on the different amino acid metabolism in cancer tissue and normal tissues. 11C-met is probably the best tumour detector and quantitative evaluation of its uptake is possible. We used 11C-met in monitoring treatment response in clinically evaluable breast cancer metastases. Nine patients with soft tissue (lymph nodes, lung, pleural) metastases were studied twice: before the onset of chemotherapy (five), hormonal treatment (three) or radiotherapy (one) and 1–2 months later. The dosage of 11C-met was 6–9 mCi. An ECAT Scanner (931/08-12) was used for PET imaging. Venous blood samples were centrifuged and the radioactivity of the plasma samples and gel filtrated samples for the low molecular weight fraction of plasma was counted. The metastases were clearly detectable with 11C-met. The input corrected uptake of 11C-met seemed to correlate with the clinical response to therapy: the uptake decreased or remained stable when clinical response or stability was obtained. 11C-met in PET imaging provides a useful method in monitoring treatment response and studying tumour viability in breast cancer.

A comparison of ^{99}Tc^{m} dimercaptosuccinic acid and micturating cystourethrogram in the investigation of children with proven urinary tract infection

F. V. Gleeson and I. Gordon
Department of Radiology, The Hospital for Sick Children, Great Ormond Street, London WC1, UK

Children aged between 1 month and 5 years referred to a district general hospital with urinary tract infection who underwent an ultrasound (US), micturating cystourethrogram (MCU), and ^{99}Tc^{m}-dimercaptosuccinic acid (DMSA) within a 4 week period were included in the study. Children with an anatomical abnormality on US were excluded, leaving 50 children with 100 kidneys for analysis. The aim of the study was to determine the correlation between the incidence of vesicoureteric reflux (VUR) on MCU, and renal scarring on DMSA. There were 18 boys and 32 girls. Of the 100 kidneys studied, 21 were scarred, and reflux identified in 36. There were eight scarred kidneys not associated with reflux, and 24 kidneys in which there was reflux but no scarring. Sixty-six per cent of those kidneys associated with reflux were not scarred, and 38% of the scarred kidneys were not associated with reflux. This suggests that the detection of VUR is in itself not as important as the detection of a scarred kidney. From this one would suggest that the MCU should be reserved for those children over 1 year old who have an abnormal DMSA scan and so require long-term antibiotic therapy.

Metastatic squamous carcinoma in the neck: an anatomical and physiological study using computerized tomography and single-photon emission computerized tomography ^{99}Tc^{m}(V) dimercaptosuccinc acid

J. C. Watkinson, C. R. Lazarus, C. Todd, M. N. Maisey and S. E. M. Clarke
Department of Otolaryngology, Guy's Hospital, St Thomas' Street, London SE1 9RT, UK

Technetium 99m(V) dimercaptosuccinic acid (DMSA) is a new tumour imaging agent which has been used to image squamous cell carcinoma (SCC) of the head and neck. This study has been undertaken to compare clinical examination with computerized tomography (CT) (anatomical) and single-photon emission computerized tomography (SPECT) ^{99}Tc^{m}(V) DMSA (physiological) imaging in the evaluation of metastatic SCC of the neck. Twenty-five patients with head and neck cancer were studied. Computerized tomography was as sensitive (71%) but more accurate (79% versus 72%) than clinical examination in predicting which necks contained cancer. Single-photon emission computerized tomography ^{99}Tc^{m}(V) DMSA was inferior to both techniques in identifying which necks contained metastatic disease (59% sensitivity, 62% accuracy). There is no role for SPECT ^{99}Tc^{m}(V) DMSA imaging in the management of patients with metastatic neck SCC. Combined imaging with CT offered no advantages over anatomical imaging with CT alone. There is no role for CT in the routine evaluation of the clinically N_0 neck, and the role of neck CT in the management of patients with metastatic SCC is discussed.

Value of magnetic resonance imaging in recurrent medullary cell carcinoma of the thyroid: comparison with pentavalent ^{99}Tc^{m} dimercaptosuccinic acid scintigraphy

R. Chaudhuri, S. E. M. Clarke and J. B. Bingham
Departments of Radiology and Nuclear Medicine, Guy's Hospital, London SE1 9RT, UK

Medullary cell carcinoma of the thyroid (MCT) is a rare tumour (2–9% of thyroid malignancies). Diagnosis of metastases is important as survival may be prolonged if treatment is appropriate. Pentavalent technetium 99m dimercaptosuccinic acid (^{99}Tc^{m}(V) DMSA) has 84% sensitivity for detection of functioning lesions in MCT, including in soft tissues and bone. Six patients, all of whom had had previous surgery and now had biochemical evidence of recurrent MCT, were evaluated with whole body ^{99}Tc^{m}(V) DMSA scintigraphy and magnetic resonance (MR). T_1- weighted spin echo and short tau T_1 inversion recovery sequences (STIR) were used in all patients but one in multiple planes. The neck and chest were imaged, and in two cases the abdomen and pelvis were also examined. All patients showed altered signal on MR in all areas of abnormal **99Tcm(V)** DMSA uptake. One (17%) had exact correlation between the number of abnormal areas and the number of lesions with both techniques. Three (50%) had the same number of abnormal areas identified, but MR resolved more foci and extent of invasion within those areas. Two (33%) each showed a single area of uptake on scintigraphy, but seven and 11 areas of disease on their respective MR scans, including lesions to liver, lung, soft tissue and bone, which were not located on **99Tcm**(V) DMSA scanning. Our findings indicate that MR, particularly with STIR sequences, has superior spatial resolution and improved lesion detection in MCT, and is a valuable alternative screening test to **99Tcm** (V) DMSA scintigraphy, especially when surgery is contemplated.

Gallium 67 citrate scintigraphy in the investigation of human immunodeficiency virus positive patients with pyrexia of undetermined origin

J. R. Buscombe, R. F. Miller and P. J. Ell
Institute of Nuclear Medicine and Academic Department of Medicine, University College and Middlesex School of Medicine, London W1N 8AA, UK

Human immunodeficiency virus (HIV) positive patients often present with pyrexia but no localizing signs. In the first UK prospective trial, 25 HIV positive patients who had suffered persistent pyrexia of undetermined origin for at least 7 days were studied using gallium 67 citrate (^{67}Ga) scintigraphy. The aim of this study was to determine if ^{67}Ga scintigraphy should be the first investigation of choice in these patients. Whole body images were performed between 24 and 72 hours post injection of 200 MBq of ^{67}Ga citrate. All results were then correlated with the final diagnosis found using microbiological, histopathological and other radiological techniques. Twenty-five sites of infection were identified in 14 patients all of whom were imaged with ^{67}Ga. Of the sites positively identified as infective, 13 were in the chest. Ten patients had focal uptake which was not due to infection, seven were later proven to be due to lymphoma. Twelve patients had colonic uptake but no infection could be localized in the bowel. The high sensitivity of ^{67}Ga makes this the ideal methodology for first use in this patient group but any site of focal uptake must be fully investigated.

Arterial oxygen saturation during isotope perfusion scans using macroaggregates of albumin

S. A. Renowden and M. W. J. Hayward
Department of Diagnostic Radiology, University of Wales College of Medicine, Cardiff CF4 4XN, UK

Ventilation perfusion (VQ) scanning using radioactive particulate matter is a widely used, safe and effective method of diagnosing pulmonary embolism. Complications are very rare and deaths confined to those patients with severe chronic pulmonary arterial hypertension. Previous studies have failed to show a significant drop in arterial saturation during lung scanning. However, using pulse oximeters it is not possible non-invasively to detect rapid changes in P_{O_2}. We studied 45 patients undergoing lung scanning. Oxygen saturation was measured at rest, following xenon 133 inhalation, and at 5 minute intervals following the injection of particles of macroaggregated albumin. Three patients showed a significant drop of 8–16%, 11 patients demonstrated a moderate decrease of 4–5% with a further 14 patients dropping slightly by 2–3%; 16 patients showed no change. Recovery occurred within 30 minutes. All patients remained asymptomatic. This finding may be of importance in patients with severely impaired lung function. The likely mechanisms involved are discussed.

An audit of non-diagnostic bone scans

S. A. Worthy and C. T. Gibson
Regional Medical Physics Department, Dryburn Hospital, Durham DH1 5TW, UK

A 5-year follow-up study of non-diagnostic bone scans in patients with extraosseous malignancy is presented. Non-diagnostic bone scans were defined as one or more abnormalities not definitely attributable to metastatic disease or other pathology. All the equivocal bone scans between 1982 and 1984 were reviewed in order to determine the proportion in which non-specific abnormalities were subsequently shown to be metastases and also the extent to which this group had been further investigated. Attributing a malignant cause to an abnormal focus of uptake has serious prognostic and therapeutic implications. This consideration, together with the non-specific nature of bone scan abnormalities, has led to a high incidence of non-diagnostic bone scan reports. Many of the group with non-specific bone scan abnormalities were subsequently shown to have had metastatic disease.

^{99}Tc^{m} radio-pharmaceuticals for the X-ray fluorescence assessment of gold *in vivo*

J. Shakeshaft and S. Lillicrap
Wessex Regional Medical Physics Department, Royal United Hospital, Bath BA1 3NG, UK

X-ray fluorescence is now a fairly well established technique for the determination of heavy metals *in vivo*. The use of external radioisotope and X-ray sources is well documented. There is, however, another possibility for organs lying at a depth, which is to use a radio-labelled pharmaceutical which is specific to the organ of interest, such as those used for imaging in nuclear medicine studies. A feasibility study of using ^{99}Tc^{m} labelled radio-pharmaceuticals as an *in situ* radiation source is presented. The work is divided into two sections. Firstly, a measurement was made to establish the activity that would be required in the kidney of a patient to achieve acceptable detection levels. Secondly, typical kidney activities were estimated in patients who were undergoing nuclear medicine studies in order to assess whether sufficient activity was present for X-ray fluorescence studies. Initial results look promising and it is hoped to develop a clinical system that will be capable of detecting levels as low as 50 μg gold per gram of kidney tissue using this technique at typical kidney depths. It is anticipated that the effective dose equivalent for such a study will not exceed 1 mSv even at kidney depths of 60 mm.

Notes

4.15 - 5.30

Silvanus Thompson Memorial Lecture

Oxford Room

Striking a balance: benefit and risk in man's exposure to man-made radiation

R. J. Berry
British Nuclear Fuels plc, Risley, Warrington WA3 6AS, UK

Beyond its initial curiosity value, and obvious benefit in the location of foreign bodies in military medicine even in the 1890s, medical radiology quickly established its benefit in diagnosis and management of a broad range of diseases. The balance of those benefits has changed however; mass screening must be justified by a sufficient pick up rate and by demonstrated benefit to the individual from early diagnosis. The use of sophisticated modern imaging techniques in managing disease in an individual must be justified by real improvement in outcome or life quality. The "risk" side emerged more slowly; deterministic (non-stochastic) damage was seen within weeks of Roentgen's discovery of X-rays in 1895 and has been eliminated from modern diagnostic radiological practice and optimized in modern radiotherapy. Understanding of long term stochastic risks was slower to develop, but is now quite advanced, particularly in regard to *medical* uses of man-made radiations. Although medical uses are the largest contributor by *dose* to exposure to man-made radiations, their *risk* is in part limited by the fact that the majority of such radiation exposure occurs late in life and often during final illness. However, public perception of risk may lead to pressure, either individual or collective, for inappropriate reduction in the use of radiation in medicine. An even wider disparity between perception and the reality of risk from man-made radiation is apparent in public attitudes to other civil uses of it, such as the nuclear power generation industry. It is argued that its benefits are under-valued and its risks both in normal operation and under accident conditions are uniquely well understood and far less to be feared than is the common perception.

Notes

Wednesday 1 May

9.00 – 10.15

Uroradiology

Clarence Room

Magnetic resonance imaging and spectroscopy of the normal and transplant kidney

A. K. Dixon
Department of Radiology, University of Cambridge, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK

Some of the techniques available for performing magnetic resonance imaging and spectroscopy (MRIS) of the kidney are described. The clinical applications are reviewed. In particular, the potential role of MRIS in renal carcinoma is considered in the context of other readily available imaging procedures. Optimal imaging parameters for studying the transplant kidney on a 1.5 T system are discussed, along with the development of STEAM spectroscopy of the renal parenchyma. The differences in corticomedullary patterns between healthy and poorly functioning renal transplants are shown. The characteristic spectroscopic findings are discussed.

Detection of non-palpable testes by magnetic resonance imaging

C. Kaniklides, P. Pech, T. Lönnerhold and J. Eugensvold
Department of Diagnostic Radiology, University Hospital, S-751 85 Uppsala, Sweden

Pre-operative localization of non-palpable testis is helpful in planning the surgical approach. Many methods have been used with varying success to locate the undescended testis. Magnetic resonance (MR) imaging was performed in 19 patients (3–12 years old), 17 with unilateral and two with bilateral cryptorchism. All of the patients underwent imaging in both the axial and coronal planes with short and long TR/TE sequences using a 0.5 T Siemens Magnetom and either body or head coil. Surgical and histological findings were correlated with MR reports. In 16 cases there was a complete agreement between MR and surgical findings. In two cases both MR and surgery were negative. The undescended testes were found either in the pelvis (four cases) or were intracanicular (six cases). In two patients, MR imaging suggested atrophic testicular tissue but at operation lymphatic nodula or epididymal-bitestical tissue were found respectively. The undescended testis was most confidently identified in the axial plane as a round or ovoid structure, with best testis–fat contrast at T_2-weighted images. The inguinal canal was best identified at T_1-weighted images in the coronal plane. In our opinion MR imaging is a sensitive modality in the localization of undescended testes.

Percutaneous nephrostomy in the management of upper urinary tract obstruction

T. R. Terry, E. Kehinde, Z. Butt, Y. Reese and E. Watkin
Departments of Urology and Radiology, Leicester General Hospital, Leicester LE5 4PW, UK

A review of percutaneous nephrostomy (PCN) performed at Leicester between January 1988 and June 1990 was carried out to identify the nature and incidence of morbidity and the case mix of patients. Percutaneous nephrostomy was performed on 85 kidneys in 73 patients with a mean age of 56.7 years and range 14 – 85 years. The underlying pathology was stone disease 35.5%, malignancy 24.5%, benign ureteric strictures 15%, PUJ obstruction 12% and idiopathic retroperitoneal fibrosis 8%. A dilated non-obstructed upper tract was present in 5%. Percutaneous nephrostomy resulted in one death from sepsis and the placement of one PCN failed. Minor complications of PCN were catheter blockage (n=13), catheter displacement (n=6), sepsis (n=2) and haemorrhage (n=2). The mean duration of PCN drainage was 21.5 days (range 2–90). The mean survival time for cases of malignant ureteric obstruction was 5.4 months. Percutaneous nephrostomy was permanent in three patients but in 20 kidneys internal ureteric stents replaced PCN. The overall nephrectomy rate was 8% (7/85). The present study confirms that PCN is an effective and relatively safe method of providing temporary or prolonged urinary diversion in the management of obstructive uropathy. Its use in pelvic malignancy should be individualized by the likelihood of obtaining worthwhile prolonged palliation.

Follow-up of adults with haematuria and negative urography and ultrasound

T. M. M. Meagher, J. Spencer and D. R. Lindsell
Department of Radiology, John Radcliffe Hospital, Oxford OX3 9DU, UK

One hundred and fifty-five consecutive adults referred from local general practitioners and hospital outpatient departments for investigation of haematuria were examined prospectively and concurrently with ultrasound and urography. Patients with proven associated urinary tract infection, acute loin pain or trauma were excluded. For 44 patients the cause of haematuria was found on initial radiological assessment: 20 bladder tumours (four seen only by ultrasound), two renal tumours and 14 with urinary tract calculi. The 111 patients with normal findings or only minor radiological abnormalities have been reassessed at a minimum of 1 year follow-up by assessment of case notes and questionnaires to their general practitioners. Thus far only 31 of these patients (28%) have been cystoscoped with detection of three small "plane" bladder tumours. One patient passed a previously undiagnosed calculus. These findings indicate that progression to cystoscopy after initial negative radiological assessment cannot be assumed and reinforces the need for accurate imaging of the bladder, by far the commonest site of malignancy resulting in haematuria. Ultrasound of the bladder should be performed as part of all radiological assessments for haematuria.

Is bowel preparation necessary before intravenous urography?

C. D. George, S. J. Vinnicombe, A. Balkissoon and C. W. Heron
Department of Radiology, St George's Hospital, London SW17 0QT, UK

Controversy exists as to whether or not bowel preparation before intravenous urography (IVU) is necessary. We present data from a study designed to test the hypothesis that adequate bowel preparation before IVU facilitates a superior quality study, requiring fewer radiographs and shorter examination times. Two hundred patients attending for IVU were randomized to receive either no bowel preparation or picolax. The number of radiographs taken and the duration of the procedure were recorded. Radiographs were scored "blind", by three radiologists, for adequacy of bowel preparation, clarity of the renal tracts and cause of reduced clarity, *i.e.* gas or faeces. Of 51 studies completed to date, 28 received no preparation and 23 picolax. Bowel preparation was considered adequate as the faecal contamination score was significantly lower in the picolax group. There was no significant difference between the groups when scored for renal tract clarity. Faeces reduced clarity in the unprepared group and gas in the picolax group. It was found that in gas-filled colon, prominent haustra and bowel wall obscured visualization. We conclude that thorough bowel preparation does not reduce the number of radiographs taken, shorten examinations or improve renal tract clarity. Data on all 200 patients will be presented.

The antenatally diagnosed multicystic kidney and the role of post-natal imaging

F. V. Gleeson, S. M. Zappla, R. A. Risdon, I. Gordon, H. K. Dillon, P. G. Duffey and P. G. Ransley
Department of Radiology, The Hospital for Sick Children, Great Ormond Street, London WC1, UK

One hundred children with the diagnosis of multicystic kidney were assessed. The diagnosis of multicystic kidney was made either from the classical ultrasound appearances with nuclear medicine correlation, or following surgical removal. All the children had been referred to the Hospital for Sick Children between 1980 and 1989 following antenatal diagnoses of hydronephrosis in 32 cases, multicystic kidney in 66 cases, and a renal mass in two cases. The median gestational age of detection of a renal abnormality by antenatal ultrasound was 30 weeks. Multicystic kidney was more common in boys than girls, 63:37, and slightly more common on the right than the left, 57:43. Post-natal ultrasound examination demonstrated additional abnormalities in 51 patients, the most frequent abnormality being contralateral hydronephrosis present in 24 cases. There was an associated ipsilateral ureterocoele in 10. The cystic dysplasia was limited to the upper moiety of a complete duplication in five. Micturating cystourethrography (MCU) revealed abnormalities in 37, including vesicoureteric reflux in 17. Overall genitourinary abnormalities were detected in 75 patients when the ultrasound and MCU investigations were combined. Nuclear medicine demonstrated unequivocal function in one case. Our series of 100 cases shows that a careful post-natal ultrasound examination should be performed in all instances of renal abnormality detected antenatally, both to confirm the initial diagnosis, incorrect in 34 of our cases, and to detect the associated renal tract abnormalities, present in 51 of our patients.

Investigation of voiding function and dysfunction following enterocystoplasty

*J. Noble, *T. Christmas, D. Kessell and D. Rickards
*Departments of Radiology and *Urology, The Middlesex Hospital, London W1N 8AA, UK*

Entercystoplasty is indicated for substitution or augmentation of the urinary bladder. Post-operative assessment of neo-bladder function can be performed by ultrasound cystodynamogram (USCD) or video-cystometrography

(VCMG). Forty-three patients have been investigated following caecocystoplasty (n=25), colocystoplasty (n=8) and "clam" ileocystoplasty (n=10). The indication for cystoplasty was detrusor hyperreflexia (n=28), interstitial cystitis (n=7), tuberculous cystitis (n=2) and radiation cystitis (n=6). 26/43 (60%) of these patients voided completely on USCD/VCMG with intermittent flow rates due to abdominal straining. 13/43 (30%) patients left residual urine volumes of greater than 200 ml: four due to outflow obstruction which was relieved surgically and nine without obstruction who were treated by intermittent self catheterization. The remaining 9/43 (10%) patients demonstrated high pressure bowel segment peristaltic contraction on VCMG necessitating detubularization. USCD/VCMG are thus important in the post-operative assessment of entercystoplasty and the relative indications and merits of both procedures will be discussed.

Computed tomography in primary aldosteronism

P. Sanville and J. E. Adams
Department of Diagnostic Radiology, University of Manchester, Manchester M13 9PT, UK

Primary aldosteronism is a rare cause of hypertension. The aetiology may be either an adrenal adenoma or bilateral adrenal hyperplasia. Differentiation between these two aetiologies is essential, since removal of the adenoma is curative, but adrenalectomy is ineffective in bilateral adrenal hyperplasia. During the 6 year period 1984–1990, 12 patients with primary aldosteronism were referred for computed tomography (CT). The majority of the patients had a long clinical history (mean 7 years) of vague and non-specific symptoms, and a moderate to severe labile hypertension. One patient suffered a cerebro-vascular accident. All had confirmed biochemical evidence of excess aldosterone production. Eight patients were treated surgically. Unilateral adenoma were confirmed to be present in seven (one multiple requiring repeat surgery). In the remaining patient, there was adrenal hyperplasia. One patient with a unilateral adrenal mass on CT refused surgery: this patient and the remaining three patients were treated medically. Computed tomography identified all the unilateral adrenal tumours (eight). The adenomas were small (mean diameter 1.7 cm) and of low attenuation (mean -1 HU) with some enhancement following intravenous contrast medium (mean post-contrast attenuation +35 HU). In the four cases of hyperplasia, CT was initially reported as bilateral adrenal enlargement (two) or "normal" adrenals (one), confirming or implying hyperplasia. In one patient unilateral adrenal enlargement was reported, the contralateral gland being considered normal. At surgery, hyperplasia was confirmed, and on careful review of the CT examination subtle abnormalities were confirmed in this contralateral adrenal consistent with hyperplasia. Hyperplastic adrenal glands had a significantly ($p<0.05$) higher attenuation (27 HU) than the attenuation of the contralateral normal adrenal gland (17 HU) in patients with adenomas. The hyperplastic glands had a significantly greater maximum cross-sectional area (2.18 cm^2) than the normal adrenal glands in the adenoma group (1.04 cm^2) ($p<0.05$). Our study confirms that CT is a reliable method for identifying unilateral Conn's tumours, but attention to scanning technique (thin, 5 mm contiguous sections) is imperative to avoid small tumours being missed. Careful scrutiny of the size and shape of the adrenals is essential to identify correctly bilateral nodular hyperplasia and so avoid unnecessary and unhelpful surgery.

Congenital urethral hypoplasia

F. V. Gleeson, J. Somers, D. G. Shaw and P. G. Ransley
Department of Radiology, Hospital for Sick Children, Great Ormond Street, London WC1, UK

Urethral hypoplasia is a rare congenital anomaly hitherto undocumented in the radiological literature. It is usually localized to the bulbar urethra, and may be associated with other severe congenital anomalies such as prune belly syndrome. We report on a group of children with urethral hypoplasia diagnosed whilst being investigated following an antenatal diagnosis of hydronephrosis. The findings at micturating cystourethrography, urethroscopy, and retrograde urethrography are described.

Anomalous penile venous drainage in erectile dysfunction

P. D. Miller, T. J. Christmas, D. Rickards and R. S. Kirby
Department of Urology and Radiology, St Bartholomew's and Middlesex Hospitals, St Bartholomew's Hospital, London EC1A 7BE, UK

In order to study the penile venous anatomy in patients with erectile dysfunction due to venous leakage, we have performed cavernosography in over 80 patients. Cavernosography confirms that the main venous drainage of the corpora cavernosa is via the cavernous, crural and deep dorsal veins. These are the most common sites of leakage in patients with venogenic impotence. However, there are a small group of patients whose erectile dysfunction appears to be due to leakage along anomalous venous tributaries. We present 10 cases where we have demonstrated anomalous penile venous anatomy, including drainage into a varicocele and into the long saphenous vein. Ligation of these anomalous tributaries resulted in restoration of potency. Non-invasive methods, such as the colour Doppler, for the diagnosis of venous leakage are now available. However, these cases demonstrate that detailed knowledge of the penile venous system and cavernosography are still essential for the proper diagnosis and treatment of patients with venogenic impotence.

The radiology of urethral stents

D. Rickards, J. Donald and *E. Milroy
*Departments of Radiology and *Urology, The Middlesex Hospital, London W1N 8AA, UK*

Urethral strictures are common and traditionally treated by dilatation or optical urethrotomy. Stricture recurrence is also common despite treatment by repeated dilation and urethrotomy, and formal urethroplasty is undertaken as a curative measure. Self-expanding metal stents are emerging as an effective and minimally invasive alternative therapy. We report the radiological appearances in 33 patients with recurrent sub-prostatic urethral strictures in whom the Urolume stent has been inserted. Pre-insertion urethrography detailed the site and length of the stricture, the appearance of the rest of the urethra and any other pertinent pathology. Post-operative urethrography at 1, 3, 5 and 12 months documented the calibre of the intrastent urethra, recurrent strictures and their sites, and was compared with the appearances at cystoscopy and flow rates. All the strictures have been successfully treated. In 19 patients, the first post-procedural urethrogram showed irregular narrowing of the intrastent lumen due to hyperplasia. The flow rates in these patients were satisfactory. Post-operative stricturing was seen in 14 patients, eight due to initial misplacement, and was successfully treated by additional stents. Two patients have developed significant new stricturing within the stent and four very near the stent. The significance and appearance of these complications will be discussed.

Notes

9.00 – 10.15

Quality Assurance in Radiotherapy

Balmoral Room

Quality assurance in radiotherapy

S. Williams
School of Therapy Radiography, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, UK

This paper will outline how a guidance document on Quality Assurance in Radiotherapy (QUART) has been formulated in an attempt to introduce systematic quality assurance procedures in all radiotherapy departments in the country. In January 1989, the Standing Sub-Committee on Cancer agreed to establish a Working Party on Quality Assurance in Radiotherapy. The terms of reference for the working group were: (1) to consider the national implications of the Thwaite Report and to make recommendations; (2) to consider the methods for ensuring accurate and reproducible treatment for an individual patient on a day to day basis and to make recommendations. A small subsection of this working party finally evolved and their task was to constitute a guidance document for radiotherapy presented in the format of the British Standard Institute Quality System Specification 5750. The QUART Standard so constructed sets out 18 requirements to be satisfied plus guidelines to assist every radiotherapy department to produce its own Quality Assurance manual based on this Standard. Some of the problems of adapting a document initially designed for the manufacturing industry to quality assurance for patients will be mentioned, in addition to the recurring problems of trying to achieve uniformity of standards without being over-prescriptive and without causing major financial implications.

Quality assurance in radiotherapy: clinical aspects

R. G. B. Evans
Department of Radiotherapy, Newcastle General Hospital, Newcastle upon Tyne NE4 6BE, UK

Quality assurance is recognized as an important part of the service provided by a radiotherapy department. The selection of patients, the choice of method of treatment, the prescription and the monitoring of the clinical outcome are the responsibilities of the radiotherapists and clinical colleagues; Clinical Audit is outside the remit of the guidelines proposed by the Department of Health's Quality Assurance in Radiotherapy document. However, the more general aspects of the conduct of a radiotherapy service are also the responsibility of a team within a radiotherapy department and these will be described. A systematic approach to quality assurance is now possible in all departments and this will provide a background on which improvements in care can be assessed. Included in the paper are aspects of the service; examples of good practice, from pre-treatment evaluation through the treatment process to the final discharge of the patient, will be given.

Quality assurance in radiotherapy: physical aspects

P. C. Williams
North Western Medical Physics Department, Christie Hospital, Manchester M20 9BX, UK

Systematic quality assurance in radiotherapy can be improved by following the guidance prepared by a multidisciplinary Department of Health working party. In the past, it has been recognized that high standards in the physical and technical aspects of the service are prerequisites of successful radiotherapy. To this end, systems of quality control involving inspection and testing of facilities have been developed to meet the needs of individual departments. Unfortunately, this essential quality control has often been assumed to encompass the whole of quality assurance. This is not the case. The basic requirements of a systematic quality assurance program are common to the physical, clinical and radiographic aspects of a radiotherapy service. The interpretation of each requirement reflects the particular processes for which each group is responsible. Some examples of methods of meeting the requirements in the context of radiotherapy physics activities are presented. It is demonstrated that, although implementation of the guidance will have initial resource implications, many benefits will accrue. All processes which have an impact on the quality of the service have to be carefully specified and subsequent monitoring of the organization's performance against these specifications will, in the longer term, enable managers to improve the services that they deliver.

Quality assurance in radiation therapy

D. Belfour and P. deSilva
Radiation Therapy Services, London Regional Cancer Centre, London, Ontario N6A 4L6, Canada

The delivery of radiation for the treatment of malignant disease impacts on a significant number of consumers and has forced many institutions and organizations to produce identifiable methods of assuring quality of care. Health care consumers in Canada are informed and educated about available services and standards of care. They are willing to "shop around" to obtain what they see as the best technical and emotional care obtainable. Many are unwilling to make compromises. The consumer must feel confident in the ability to communicate with any member of the health care team at any time before, during or after the treatment process. All staff members must be actively listening to their patients and be prepared to follow up every concern or complaint raised. This educational poster displays some of the methods employed for auditing and monitoring radiation treatment delivery in a radiation therapy department. The three areas covered are as follows: (1) accurate recording and delivery of radiation treatments on a daily basis; (2) adequate standards of patient care; (3) departmental standards expected of the radiation therapy technologists. Outcomes of these reports must be reviewed monthly, trends must be identified and changes must be implemented as appropriate to achieve acceptable standards of care.

Initial experience of megavoltage imaging for breast treatment verification

M. C. Kirby and P. C. Williams
North Western Medical Physics Department, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, UK

Current advances in external beam radiotherapy demand more accurate, versatile and precise methods of treatment verification. A step in this direction is the use of digital, on-line portal imaging during treatment. At the Christie Hospital, a Philips SL25 linear accelerator has been recently equipped with a multileaf collimator and a commercially available fluoroscopic, on-line megavoltage imaging (MVI) system (Philips SRI 100). A primary clinical evaluation of the MVI system has centred on standard treatment techniques, one of which is the treatment of breast malignancies. Here the collimator can produce asymmetric fields in order to achieve perfect matchlines for abutting treatment fields and to effect a greater degree of lung sparing. Presented are the results of this evaluation. High quality images are obtained from the MVI system especially in terms of soft tissue and lung detail; this is a considerable improvement on traditional portal films. Comparison is made with pre-treatment simulator images and computed tomography scans to validate patient treatment set-up. Day-to-day changes in set-up can be quantitifed as can parameters such as depth of lung and soft tissue irradiated. The MVI system has rapidly established itself as an important part of breast radiotherapy treatment, producing versatile, high quality verification images and also quantitative clinical information.

Use of predefined shapes for producing irregular fields with a multileaf collimator

P. C. Williams and B. Kane
North Western Medical Physics Department and Radiotherapy Department, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, UK

The Philips multileaf collimator has 80 leaves in two opposing banks which can be positioned to project irregular field shapes up to 40 cm x 40 cm in the isocentric plane. There are three modes of operation. The first emulates a conventional collimator and allows for rectangular fields, which may be offset relative to the central axis, to be produced. The second allows individual leaves to be set to allow for any irregular shape to be produced but this requires the input of 80 values describing the leaf positions. The third mode allows a series of pre-defined shapes to be produced with the limitation that each shape can be defined by no more than eight parameters. These shapes can be scaled by altering the values of these parameters either via keyboard entry or continuously using thumbwheel controls on the collimator cover. A study has been carried out to assess how well the blocked fields for a series of treatments could have been produced with the multileaf collimator rather than with blocks on a shadow tray. The results demonstrate that many shaped fields can be produced with this simple yet versatile facility.

Performance characteristics of the Philips multileaf collimator

P. C. Williams and T. J. Jordan
North Western Medical Physics Department, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, UK

A prototype multileaf collimator has been commissioned for clinical use on a Philips SL25 linear accelerator in order to facilitate the development of conformal therapy. The collimator is designed to produce regular and irregular fields without compromising the use of the accelerator for conventional X-ray or electron therapy. The results presented show that the system has met its design criteria in respect of radiation leakage, X-ray beam penumbra and positional control. Leakage through the collimators is acceptably low and for rectangular fields complies with the requirements set out in British Standards. The penumbra for fields defined by the multileaf collimator compares favourably with that for a conventional four-block collimator and shows only small variation with field size and photon energy. The control system is shown to be able to position the leaves to within 1 mm of the prescribed value and to be able to move the leaves to the prescribed position rapidly. The basic beam performance, uniformity and quality are unaffected by the multileaf collimator.

Notes

9.00 – 12.00

Consensus Workshop: The management of bone tumours

Lancaster Room

Chairman: Dr D. J. Stoker, Clinical Radiologist
Panel: Professor R. L. Souhami, Oncologist, Dr Jean Pringle, Histopathologist and Mr S. R. Cannon, Orthopaedic Surgeon
The London Bone Tumour Service, Royal National Orthopaedic and Middlesex Hospitals, London, UK

This workshop is conducted by a team working together in a Supra-Regional Bone Tumour Service formed for the treatment of primary tumours of bone and with a particular objective of limb salvage whenever possible rather than amputation. The workshop aims to examine questions of concern relating to the epidemiology of this form of cancer, as well as diagnosis, cytotoxic and surgical treatment. During the course of the programme, while imaging methods will remain in the forefront in terms of early management and staging, stress will be laid on the cooperation and inter-relationship between the members of the team. We also wish to address the funding and economics of such supra-regional initiatives and whether the benefit to the patient is proven and paramount. The object is to raise provocative issues and thereby to stimulate participation by the audience.

9.00 – 10.15

Cardiovascular Imaging

Norfolk Room

Ultrasound of the heart

P. Wilde
Department of Radiodiagnosis, Bristol Royal Infirmary, Bristol BS2 8HW, UK

A review of current cardiac ultrasound technology will be given. All imaging and Doppler modalities will be discussed. Particular emphasis will be given to Doppler quantitation of haemodynamic abnormalities, colour flow mapping and transoesophageal echocardiography. A range of clinical examples will be given showing the use of these techniques in both adult and paediatric cardiological practice. Cardiac ultrasound diagnosis will be compared with other non-invasive cardiac imaging modalities.

Transeptal balloon mitral valvoplasty: initial results using the Inoué technique

E. F. Brown, *T. MacConnell, *J. C. Pitts Crick and G. G. Hartnell
*Departments of Radiodiagnosis and *Cardiology, Bristol Royal Infirmary, Bristol BS2 8HW, UK*

Conventional percutaneous balloon mitral valvoplasty is difficult and may not produce good results. The difficulties in introducing balloons of a sufficient size and maintaining a stable position across the valve may limit its application. We report our initial experience with the use of a single balloon device specifically designed for balloon mitral valvoplasty (Inoué balloon). Seventeen patients (15 female, mean age 58.7 years) with mitral stenosis and little or no regurgitation underwent transeptal valvoplasty using the Inoué balloon. Mean valve area measured by echocardiography rose from 0.96 cm^2 to 1.58 cm^2 with valve area more than doubling in the majority of cases, with commensurate changes in valve gradients. There was a significant increase in mitral regurgitation in only one. One procedure was abandoned due to incorrect balloon assembly. No clinically significant atrial septal defects occurred. The method, patient selection and important points of the technique will be illustrated. Early experience suggests that mitral valvoplasty using the Inoué balloon produces good results in the majority of patients. It is a good alternative to surgery for mitral stenosis and does not preclude valve replacement.

Diseases of the thoracic aorta: comparison of magnetic resonance imaging with transoesophageal echocardiography and angiography for diagnosis

R. MacMillan and K. Chandrasekaran
Department of Medicine and Radiology, Hahnemann University Hospital, Philadelphia, PA 19102, USA

Ten patients, one female and nine male, mean age 55 years (range 16–79 years) had magnetic resonance imaging (MRI) performed using a 1.5 T GE signal system. Multilevel, 10 mm thick ECG-gated T_1 spin echo pulse sequence images were acquired at 33 ms intervals through the cardiac cycle. The matrix was 128×256, TE:20 and TR equal to the cardiac cycle in milliseconds. Images were obtained in axial plane with selected use of coronal, sagittal and off-axis planar orientations. GRASS cine MRI was performed on three patients with aortic regurgitation. Six patients had transoesophageal echocardiography (TEE) and seven had aortic angiography. Diagnoses were aortic dissection (four), ascending aortic aneurysm with severe aortic regurgitation (two), ascending aortic aneurysm with intraluminal conduit (two), coarctation of aorta (one), and aortopulmonary window (one). Magnetic resonance imaging correctly identified aortic dissection in all four patients compared with TEE and/or angiography. Three patients were correctly diagnosed with Type III dissection and one with Type II dissection. In one of two cases of ascending aortic aneurysm with aortic regurgitation, TEE reported a dissection flap, but MRI and angiography were negative and no dissection was seen at surgery. Magnetic resonance imaging agreed with TEE in both cases of aortic aneurysm with postop conduits. In one case, the conduit was observed to be compressed in its middle third, presumably by the surrounding haematoma. Magnetic resonance imaging was in agreement with echocardiography in detection and gross estimation of aortic regurgitation in all three patients found to have it. Aortopulmonary window was easily distinguished from a truncus arteriosus using MRI based on the detection of a very proximal septum between the two great vessels. We conclude that MRI is highly useful for diagnosis of diseases of the thoracic aorta. We suggest that since TEE is semi-invasive, MRI in the majority of cases is the preferred technique for non-invasive diagnosis.

Application of magnetic resonance velocity mapping to measurement of flow through healthy and stenotic mitral valves.

R. H. Mohiaddin, C. C. Manzara, P. J. Kilner,
D. J. Pennell, D. N. Firmin, M. Amanuma,
S. R. Underwood and D. B. Longmore
Magnetic Resonance Unit, National Heart and Chest Hospitals, London SW3 6NN, UK

Magnetic resonance (MR) imaging is not limited by acoustic windows and is capable of accurate blood flow velocity measurement, but it has not been previously used to assess valvular stenosis. We measured mitral blood flow using MR phase-shift velocity mapping in 10 healthy volunteers and in seven patients with mitral stenosis. Mitral flow direction was determined from a TE 14 ms FEER magnitude acquisition sensitive to signal loss from turbulence. Mitral flow velocity (TE 3.6 ms) was then acquired in two oblique planes, parallel and perpendicular to the axis of mitral flow. Magnetic resonance measurements were compared with Doppler echocardiography. Peak MR mitral flow velocity (mean±SD) in early diastole was 68±12 cm/s, and in atrial systole 39±10 cm/s with a ratio of 1.9±0.6. These agree with normal values obtained from Doppler echocardiography. In patients with mitral stenosis there was persistent flow throughout diastole, which was significantly higher than in normal patients. The average peak MR velocity measurement was 189±47 cm/s compared with the Doppler velocimetry measurement of 204±56 cm/s. The values correlated well (r=0.91). Magnetic resonance velocity mapping is a new non-invasive method for measurement of blood flow velocity through the mitral valve, characterization of its pattern and calculation of pressure half time. This technique is complementary to other non-invasive investigations for the assessment of mitral valve disease and evaluation of left ventricular diastolic function, particularly when adequate Doppler measurements are difficult.

Pulmonary scintigraphy in pulmonary embolism: how often does it change clinical management?

P. G. White, G. R. J. Sissons and M. W. J. Hayward
Department of Radiology, University Hospital of Wales, Cardiff CF4 4XW, UK

The accuracy of pulmonary scintigraphy in the diagnosis of pulmonary embolism (PE) continues to be a source of debate. The influence of this investigation, and other parameters, on clinical decision-making has been assessed. One hundred and forty-six successive patients with suspected PE underwent pulmonary scintigraphy during an 11 month period. Retrospective review of the case notes of 134 patients has shown a change in anticoagulant therapy in 35 cases (26%) following pulmonary scintigraphy. In 29 of these anticoagulant therapy was withdrawn, in five anticoagulant therapy was commenced, and in one case therapy was supplemented by a thrombolytic agent. In 99 patients (74%) there was no change in management. Sixty-six patients remained on no therapy and in 33 cases anticoagulants were continued. Amongst the latter were nine patients whose anticoagulant therapy was continued despite a normal or low probability scan result. It is clear that pulmonary scintigraphy is an important determinant of clinical management in suspected PE and often leads to withdrawal of anticoagulant therapy. However, clinical suspicion based on other parameters is the decisive factor in the management of some patients.

Magnetic resonance imaging and coarctation of the aorta: imaging structure and function

R. A. Coulden, J. P. R. Jenkins, Y. Watson and
I. Isherwood
Department of Diagnostic Radiology, University of Manchester, Manchester M13 9PT, UK

The aim of this study was to assess the role of magnetic resonance imaging (MRI), in comparison with Doppler echocardiography and aortic catheterization, in the evaluation of coarctation of the aorta. Eleven patients (aged 11–70 years) were studied with clinical coarctation or following corrective surgery. Magnetic resonance imaging was performed using a superconducting magnet system (0.26 T). Cardiac-gated multislice spin echo sequences were performed in the transverse and sagittal-oblique planes. Using the most representative oblique section of the whole aortic arch, a cine field even echo rephasing (FEER) sequence was acquired to provide information on flow. Initially, FEER sequences with TE 22 or 28 ms were used to provide qualitative data. In the last five patients, the use of a modified FEER sequence (TE 12 ms) with construction of velocity flow maps enabled absolute velocity measurements through the coarctation segment. All patients were also investigated by either Doppler echocardiography, angiography or both. The results of the various techniques were compared. Diagnostic MR images were obtained in all patients. Comparison of MRI and aortography showed close correlation in terms of lesion length, configuration and percentage stenosis. Peak velocities measured by MRI and Doppler echocardiography also compared well for values up to 3 m/s. Above this, MRI signal loss hampered velocity measurements. Magnetic resonance imaging is a reliable method for assessing aortic anatomy and function and can be used in place of aortography or when Doppler echocardiography is technically difficult. The use of shorter TE times (less than 12 ms) should allow assessment of higher peak velocities.

Quantitative magnetic resonance angiography of patients with pulmonary hypertension

E. Dinkel, Ch. Vogt, G. Würtemberger, A. Mundinger,
G. Weyrich, R. Schillinger and J. Hennig
Department of Radiology, University Clinics, Hugstetter Strasse 55, 7800 Freiburg, FRG

We sought to determine whether magnetic resonance (MR) angiography (fast Fourier flow (FFF) method) on a high field MR system (2 T) can be utilized to establish the definite diagnosis of pulmonary hypertension. The ECG-gated cine-mode requires a total acquisition time of about 1 minute, using 64 phase encoding steps in the flow direction of the 2DFT-image. Eleven patients with right heart catheter proven pulmonary hypertension due to chronic obstructive pulmonary disease and 10 healthy volunteers were studied. The maximum/mean blood flow velocity in the right pulmonary artery was 49.3(SD 6.7)/13.7(SD 2.9) cm/s in patients and 75.5(SD 20.9)/26(SD 6.9) cm/s in the healthy volunteers. Acceleration time was 109 (SD 53.2) ms in the patients and 202 (SD 47.7) ms in the healthy individuals. Volumetric flow, flow velocities and acceleration times showed considerable interindividual variations in patients as well as in healthy subjects. However, patients with pulmonary hypertension had a marked decrease in the maximum and mean flow velocity and in acceleration time in the right pulmonary artery. Thus the FFF method is a promising new non-invasive diagnostic approach in patients with pulmonary artery hypertension. More extensive studies are required to establish the reproducibility of our data in larger populations of patients with pulmonary hypertension.

Topography of deep venous thrombosis

T. Y. K. Chan and P. D. Holder
Department of Radiology, St Thomas' Hospital, London SE1 7EH, UK

Seventy patients with symptoms of deep venous thrombosis (DVT) of either or both legs underwent bilateral phlebography performed with a standard technique. The phlebograms were reviewed to define the site of thrombosis in terms of three pre-determined segments: ilio-femoral, femoro-popliteal and the calf. The presence of post-thrombotic changes (PTC) was also noted. Twenty-three patients were found to have no thrombosis on phlebograms. Of these, three had PTC unilaterally. Of the 28 patients with unilateral thrombosis, three had PTC ipsilaterally, and one contralaterally. Nineteen patients had bilateral thrombosis including one with unilateral PTC. Thrombosis was found in the right calf in 32 patients and the left in 33, in the right femoro-popliteal segment in 16 patients and the left in 17, and in the right ilio-femoral segment in 10 patients and the left in nine. Only one patient had thrombosis in the distal inferior vena cava (IVC); the thrombus extended from the left common iliac vein. Thirty-one patients had no thrombus demonstrated in the IVC. Of the remaining 38 patients whose distal cava was not demonstrated, 33 had no thrombus in either ilio-femoral segment, and five had thrombus in one ilio-femoral segment, but only confined to the common femoral vein. This study demonstrates that there is a high proportion (27%) of bilateral DVT, probably reflecting the bilaterality of the predisposing factors. The presence of PTC does not necessarily lead to thrombosis. Relative venous stasis and endothelial damage may account for the higher number (55) of DVT in the calf, compared with 33 in the femoro-popliteal segment and 19 in the ilio-femoral segmenta. There is virtually no difference in the incidence of DVT between the two legs. The significance of left common iliac vein compression syndrome does not seem to apply in our study. Direct distal IVC involvement appears uncommon. The demonstration of the distal cava may not be essential unless either iliac vein is filled with thrombus.

Abdominal aortic aneurysm – problems in computed tomography assessment of renal artery involvement

C. E. Williams, J. Meaney, J. B. Kenny, D. J. Widdowson and A. T. Carty
Department of Radiology, Royal Liverpool Hospital, Liverpool L7 8XP, UK

Initial reports on the role of computed tomography (CT) for the assessment of abdominal aortic aneurysms suggested that it was a useful means of assessing renal artery involvement. However, in many of these studies a low incidence of renal artery involvement was found and only small numbers of patients were assessed. More recently, its value has been questioned. The CT examinations in 79 patients with abdominal aortic aneurysm in whom there was a high degree of clinical and/or ultrasonic suspicion of renal artery involvement were retrospectively assessed. The majority of scans were performed using 5 mm contiguous slices with contrast enhancement. Definite involvement of the renal arteries was found in nine cases (11%) and in 49 cases (62%) the aneurysm was below the renal artery origins. However, in 21 cases (27%) it was impossible to say with any reasonable certainty using CT alone.

Use of colour three-dimensional imaging in abdominal arterial aneurysm

J. N. P. Higgins, A. D. Platts and F. Starer
Department of Radiology, Westminster Hospital, Horseferry Road, London SW1, UK

Three-dimensional (3D) images can be generated from computerized tomographic (CT) scans using software that is readily available on many CT scanners. These images are more easily interpreted than the scans from which they were derived. Colour can be used to heighten contrast between adjacent structures irrespective of their attenuation coefficients and similarly between normal structures and pathology. We present four cases of abdominal arterial aneurysm in which a colour 3D program was used to generate images from contrast-enhanced axial CT scans. In each case one or two reconstructed images provided all the information required regarding the aneurysm and associated structures in a form readily understood by both radiologists and non-radiologists. This technique represents an advance over axial CT and ultrasound which require the assimilation and interpretation of multiple images in order to build up a mental image of an abnormality.

Measurement of regional left ventricular function using labelled magnetic resonance imaging

M. B. Buchalter, C. Sims, A. K. Dixon, P. L. Weissberg, N. J. Shah, I. D. Wilkinson, D. J. Lomas and C. E. L. Freer
MRIS Unit, Addenbrooke's Hospital and the University of Cambridge, Cambridge CB2 2QQ, UK

A technique for assessing regional left ventricular function using magnetic resonance imaging is described. Spatial modulation of magnetization (SPAMM) can be effected before images are obtained at various intervals during the cardiac cycle using a modified field echo even rephasing technique (FEER). By performing such modulation in two planes, a grid pattern of labelling can be produced across the image. On the resulting labelled short-axis images of the left ventricle, the systolic increase in thickness (thickening) and decrease in length (shortening) of different regions of myocardium can then be assessed. The findings in five normal volunteers are presented. Regional circumferential shortening was twice as great in the endocardium (mean 20.4%, SD 5.7) than in the epicardium (mean 10.7%, SD 5.5). The mean percentage wall thickening was 9.8 (SD 13.5). Regional circumferential shortening offers more promise as a marker of regional function than simple thickening and should be of use in assessing areas of dyskinesia following myocardial infarction.

10.45 – 12.00

The Breast

Clarence Room

Axillary recurrence of breast cancer, a challenge for the radiologist

N. R. Moore
Department of Radiology, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, UK

Women who have had treatment for carcinoma of the breast may present later with lymphoedema or neurological symptoms. There are no reliable clinical discriminators and since the clinician may not be able to examine fully the axilla owing to scarring, it often falls to the radiologist to distinguish between fibrosis and recurrent disease. Computed tomography has been used successfully to discriminate between streaky axillary fibrosis and rounded nodal recurrence. Other features, *e.g.* lung or bone metastases, may suggest malignancy but indeterminate soft tissue masses require guided needle biopsy. Magnetic resonance imaging (MRI) can reduce the need for biopsy because it combines morphological features with an assessment of disease activity on T2 weighted spin echo images. The increasing availability may make MRI the examination of first choice. Ultrasound and scintigraphy are better than clinical assessment of nodal disease at staging, but neither has been used to distinguish fibrosis from recurrence. Ultrasound may be able to display internal nodal architecture and colour flow Doppler can detect malignant vascularity. Radiolabelled murine monoclonal antibodies which react with human breast cancer provide a new approach to disease detection. Further research is required to determine the diagnostic potential of ultrasound and scintigraphy.

Digital image processing of X-ray and magnetic resonance breast images

S. L. Free, K. Straughan, A. W. Goode, M. J. Turner, C. Panahy and R. I. Kitney
Department of Electrical Engineering, Imperial College, London SW7 2BT, UK

Breast disease, both malignant and benign, affects a large percentage of women. An X-ray mammogram is the standard examination for symptomatic women and now, via screening programmes, for asymptomatic women. There is interest in imaging techniques using non-ionizing radiation, including ultrasound and magnetic resonance imaging. Magnetic resonance, in particular, can offer physiological as well as anatomical information. The work reported here considers the extraction of diagnostically significant features from both X-ray and magnetic resonance breast images to maximize their diagnostic potential. A workstation environment has been designed for the clinical user, to enable application of digital image processing techniques to breast images from different modalities. General and feature-specific enhancement processes have been applied. Techniques from the rapidly developing area of mathematical morphology have been utilized for feature extraction purposes. These include binary and grey level erosions and openings using disk structuring elements. The image features presently considered are calcifications, the skin and lesions of varying size and shape. The measurement of feature characterisitcs includes the clustering of calcifications and shape analysis of lesions and skin. The lesion boundary can be important in determining diagnosis and can be characterized by chain codes and Fourier descriptors. Additional information can be obtained from magnetic resonance images dependent on the image acquisition protocols. This allows comparison between images of the same breast with different image parameters. Global variations of image parameters can be observed in intensity histograms, *e.g.* the shifts in water content. By considering feature characteristics in a feature space, groupings of features can be observed. Using image data sets with known diagnostic outcome, the relevance of feature groups to diagnosis can be assessed.

The assessment of screen detected mammographic abnormalities: when is the decision to operate made?

G. R. Cherryman, E. J. Roebuck, A. R. M. Wilson, I. O. Ellis, C. W. Elston and R. W. Blamey
Helen Garrod Breast Screening and Assessment Unit, City Hospital, Hucknell Road, Nottingham NG5 1PB, UK

Women are recalled from mammographic screening for the further assessment of radiological abnormalities. In a prospective study of 150 consecutive women further investigated, 41/150 women were initially referred to surgery on the basis of abnormal imaging. This lead to the recognition of 26/29 invasive cancers (PPV = 0.64). Clinical examination of the remaining 109/150 women identified one further cancer. FNAC was obtained on 15/15 palpable and apparently benign solid masses. This identified a further two malignancies. FNAC was attempted on 18/89 impalpable, but apparently benign, radiological abnormalities. No cancers were found, but an equivocal result in three women lead to diagnostic excision in one and additional needle histology in two. A decision to operate is primarily made on imaging criteria. Clinical and cytological examination will slightly improve sensitivity in the detection and diagnosis of palpable carcinomas.

A test object for evaluating the image quality of photo-stimulable phosphor computed mammography

D. S. Brettle, A. R. Cowen and N. J. Coleman
Department of Medical Physics, The General Infirmary, Leeds LS1 3EX, West Yorkshire, UK

In June 1990 we set up a programme of research to investigate the diagnostic efficiency of a mammography service based on photo-stimulable phosphor computed radiography (PPCR). To support this research we have developed a new Leeds mammography test object matched to the imaging characteristics of PPCR technology. This test object known as TOR[MAM] exhibits a variety of test details simulating microcalcifications, fibrous details and low contrast nodules. Detail detectability is evaluated against both a homogeneous and a structured background field; the latter has been designed to simulate breast morphology. This test object has been used to evaluate the image quality of our digital mammography facility both for routine quality control and specific scientific tests. Results have been compared with those produced by conventional screen-film mammography. A number of important practical issues have been identified which potentially can cause a deterioration in PPCR image quality. The test object has also proved useful in optimizing the digital image enhancement protocols used in the display of PPCR images. In this presentation we will describe our first year's technical experience with the PPCR system using results obtained with TOR[MAM] to illustrate our findings.

We are grateful to the UK Department of Health and Philips Medical Systems (UK) for their support of this project.

The combined effects of breast composition and size in determining radiation risks from mammography

A. P. Hufton, C. R. M. Boggis and M. Wilson
Department of Medical Physics and Manchester Breast Screening Service, Withington Hospital, Manchester M20 0PT, UK

In mammography, the average dose to the glandular tissues of the breast depends, amongst other things, on the composition and thickness of the breast. In addition, the risk of cancer induction must depend on the total energy absorbed in the glandular tissue, and therefore on the total volume or mass of glandular tissue. The initial aim of this study was to investigate whether there was any correlation between breast composition and thickness, and what effect this had on individual doses. This was determined by recording the kilovolts, milliamps and compressed breast thickness for 100 women undergoing mammography, and by estimating the fraction of glandular tissue from the resultant mammograms. Radiation doses were then calculated using standard techniques. The projected area of the breast was also determined from the mammograms in order to derive a simple measure of the volume of glandular tissue, and hence the total energy imparted. A weak negative correlation was found between breast thickness and glandular tissue fraction which served, on average, to reduce the doses to the larger breasts. Detailed results showing the magnitude of these effects are presented and the implications for risk evaluation in screening programmes discussed.

The predictive value of mammographic abnormalities as assessed in a screening programme

G. R. Cherryman, E. J. Roebuck, A. R. M. Wilson,
I. O. Ellis, C. W. Elston and R. W. Blamey
Helen Garrod Breast Screening and Assessment Unit, City Hospital, Hucknell Road, Nottingham NG5 1PB, UK

Mammographic abnormalities prompting recall may be considered in three groups: well circumscribed masses (WCM), poorly circumscribed masses, stellate deformities and parenchymal deformities (PCM), and clustered calcifications without other associated features (CAL). Well circumscribed masses are always considered at low risk of malignancy. In a prospective study of 150 recalls, 44 (29%) were for WCM and no cancers have been found in this group. Poorly circumscribed masses may be divided into two groups: those which remain suspicious after assessment and those, *e.g.* summation shadows, which do not. We have found 25/28 high risk PCMs to be malignant (PPV=0.89), but only 2/45 of the low risk PCMs to be malignant (PPV=0.04). Clustered calcifications are unrewarding lesions to recall and assess. We found only 2/33 women recalled with CAL to have invasive cancer (PPV=0.06). When assessed as high risk, 2/13 proved invasive tumour (PPV = 0.15), while 4/13 were DCIS and the remaining 7/13 benign biopsies. No cancer has yet been found in the group of low risk calcifications (n=20). In attempting to reduce the recall rate without reducing sensitivity it would seem sensible to minimize the recall of WCMs, think hard about recalling CALs and promote the recall of PCMs.

Small lesions in mammography: stereotactical localization for cytological puncture and histological biopsy

M. Bauer, R. Schulz-Wendtland, F. Kommoss, K. Prinz and F. Richard
Department of Gynaecological Radiology, Radiological Centre of the University of Freiburg, 7800 Freiburg, FRG

Since November 1987 we have been using, for $n = 192$ patients, stereotactical equipment compatible with the mammography system for cytological puncture, histological biopsy and pre-operative marking. After localization of the lesion with computerized help, the puncture, biopsy, and pre-operative marking is done manually. The physical exactness is ±1 mm; the maximum variation after 80 pre-operative markings is ±5 mm. By November 1990 we had carried out 112 stereotactical punctures for cytological diagnosis: a conformity of cytological and histological diagnosis was found in 82%. The advantages and disadvantages of the method will be discussed in view of their potential in breast diagnostics.

Predicting outcome in mammography: parenchymal patterns and other approaches

A. G. Gale, W. Lim, A. J. Evans, G. E. Walker and B. S. Worthington
Department of Academic Radiology, University Hospital, Nottingham NG7 2UH, UK

A retrospective investigation was carried out relating mammographic features, Wolfe classification and pathology. A randomly selected number (147) of recent positive mammograms from the Nottingham Screening Centre were reviewed for the presence of particular radiographic features and prevailing Wolfe mammographic patterns. Both lateral-oblique and cranio-caudal views were employed. Of these cases, histological information, together with a prognostic index based on these data, were available for 122, cytology alone was known for 19 cases and six were ductal carcinoma *in situ*. The prevalence of Wolfe patterns was compared with known data from other studies. The Wolfe classification was also related to abnormality type and prognostic index. Regression analysis was used to examine the relationship between mammographic features and cancer type. Finally, a predictive model for the identification of breast cancer based on the recognition of particular radiographic features as derived from a previous investigation employing symptomatic women was also tested on these data and found to be valid.

Audit in action: mammography in women under 35 with symptomatic breast disease

I. R. Brand, D. A. Sapherson and T. S. Brown
Department of Radiology, Bradford Royal Infirmary, Bradford, West Yorkshire BD9 6RJ, UK

Screening mammography for occult breast carcinoma in the over 50 age group is now widely accepted, but to date has not been of proven value in the under 50s. Little or no work has been reported in the young age group with symptomatic breast disease. One hundred and fifty-nine women with symptomatic breast disease under 35 years referred consecutively for mammography were assessed with regard to mammographic findings and subsequent clinical management. Three per cent of patients did not attend for follow-up, all of whom had no discrete mass and normal mammograms. Seventy-three per cent having mammograms had no discrete mass and in these mammography was non-contributory to the final outcome. In 24% with a discrete mass, mammography was again non-contributory, the treatment being decided on a clinical basis. Mammography therefore has no part to play in the routine investigation of symptomatic breast problems in the under 35 age group, and a protocol agreed with the surgeons has now been enacted.

In vivo localized ^{31}P spectroscopy of human breast carcinoma

J. Glaholm, M. O. Leach, D. Collins, J. C. Sharp, J. Mansi, V. R. McCready, I. E. Smith and T. Powles
Nuclear Magnetic Resonance Unit, Royal Marsden Hospital, Sutton, Surrey SM2 5PT, UK

In vivo ^{31}P magnetic resonance spectroscopy provides a non-invasive measurement of intracellular phosphorus metabolism. Serial examinations have been undertaken in 20 patients with locally advanced breast carcinoma undergoing treatment with chemotherapy, endocrine therapy and radiotherapy. Spectral information was obtained from the tumour alone using a development of the ISIS technique which localizes a cuboid or parallelepiped volume and successfully eliminates signal contamination from underlying chest wall. Signals from intracellular metabolites have been measured by relating them to a calibration sample positioned in the coil, rather than measuring metabolite ratios which often may not reflect absolute metabolite levels. Phosphomonoesters (PME) and phosphodiesters (PDE) were prominent in all of the tumours; however, phosphocreatine (PCr), which provides a high energy phosphate reserve, was undetectable or at a low level. Nucleotide triphosphates, which include ATP, and organic phosphate (Pi) were readily detected in all cases. Our results have indicated that of the intracellular phosphorus metabolites, the PME level changed most markedly in response to treatment and frequently preceeded changes in tumour volume. In human breast carcinoma, the PME peak has been shown to be composed of phospholipid precursor molecules. Phosphomonoesters may therefore reflect cell membrane synthesis and thus the rate of cell replication and promise to be a more sensitive indicator of tumour cell response to treatment than volume measurement.

Notes

Mammographic film interpretation

A. G. Gale, G. E. Walker, *E. J. Roebuck and
B. S. Worthington
*Department of Academic Radiology, University Hospital, Nottingham NG7 2UH and *Breast Screening Training Centre, City Hospital, Nottingham NG5 1PB, UK*

Trainee radiologists in screening who have attended the Nottingham training centre have had their film reading ability tested both during the multidisciplinary training course and upon subsequent secondment. A set of recent screening mammograms are employed for this task which comprise normals and abnormal cases of known pathology. During the training course, film reading is videotaped and later analysed to determine the amount of time spent per case. Examination of such data across trainees reveals the time course of film interpretation performance as assessed by ROC analysis and this is then related to the amount of time spent on film reading in practice as elicited by a national questionnaire. Comparison of data from the training course and secondment reveal differences in false positive and false negative responses. This paper further examines whether such differences are due to the effect of training and experience with mammography. Even on secondment, some positive cases are missed and normals over-read. The reason for such persistent errors are elaborated.

10.45 – 12.00

Radiotherapy Audit

Balmoral Room

Have we, can we, should we?

A. Rodger
Department of Clinical Oncology, Western General Hospital, Edinburgh EH4 2XU, UK

The new National Health Service White Paper (and now Act) "Working for Patients" laid a particular emphasis on the need to carry out medical audit. Many clinicians, and in particular clinical oncologists, would maintain that they have been involved in medical audit for some considerable time, particularly with regard to treatment outcome and treatment morbidity. While that may indeed be the case, it is unlikely that the majority of clinicians have indulged in audit of their own or their departmental practice and acted upon the results. Whether we can, given the present circumstances of our workload, lack of support staff, lack of modern computer-based management systems, and lack of designated time for audit, is questionable. Nevertheless, laying aside government dictat, it is appropriate that we should look at the question of clinical audit and decide if we should commit ourselves to such activities and to the implementation of the results of audit. The implications with respect to management, and with respect to confidentiality will be crucial. While many of us may find the jargon and the hype of medical audit somewhat difficult to accept and to enthuse over, the appropriate auditing of our work should lead to improvement in practice and therefore an improvement in our patients. This brief presentation will try to touch on each of these points in turn.

We must

C. D. Shaw
Director, Medical Audit Programme, King's Fund Centre, 126 Albert Street, London NW1 7NF, UK

All doctors in National Health Service hospital and community services are expected by the Department of Health to be involved in medial audit from 1 April this year. The Royal College of Radiologists requires audit for recognition of training posts, managers require it for service contracts – and without it, you are less likely to receive a share of the money allocated to English regions for audit (£26 million in 1990–1991). Audit is more than a formal extension to quality assurance, accreditation or radiation protection in therapeutic radiology; it requires systematic analysis of individual clinical practice against explicit standards, and the will and ability to take opportunities for improvement.

Audit in radiotherapy and oncology: what we have done

A. Hong
Royal Devon and Exeter Hospital, Exeter EX2 5DW, UK

A review has been made of all cases of head and neck cancer attending the Regional Centre for Radiotherapy and Oncology at Mount Vernon Hospital during the 8 year period from 1 January 1980 to 31 December 1987. Of 766 patients registered, a detailed analysis was made of 545 patients presenting a new primary carcinoma without evidence of distant metastases who received radiotherapy as the definitive form of treatment. The technique and intent of treatment (curative or palliative), outcome in terms of tumour control, patterns of failure, subsequent treatment and survival were examined and prognostic factors identified. The results compared favourably with those reported by other institutions, but improvements in the management of advanced disease are necessary. A comparison of these results with a group of patients treated by continuous hyperfractionated, accelerated radiotherapy had shown improved tumour control and survival in patients with advanced disease and this schedule is now the subject of a randomized controlled prospective trial. Other features of audit such as quality of life, use of resources, cost, the results of management by alternative modalities and the economic burden of failure have yet to be explored. An analysis of the audit process, time allotted and the personnel involved in each stage of this clinical audit has been made and the implications are discussed.

10.45 – 12.00

Gastrointestinal Imaging

Norfolk Room

^{99}Tc^{m} HMPAO labelled white cells in acute colitis; a comparison with plain films and air insufflation

J. Hughes, M. W. J. Hayward and *J. Rhodes
*Departments of Radiology and *Gastroenterology, University Hospital of Wales, Cardiff CF4 4XW, UK*

The extent of disease at acute presentation or exacerbation of inflammatory bowel disease (IBD) is assessed using plain films, unprepared barium enemas or air insufflation. Plain films may underestimate disease, whereas enemas are invasive and barium in particular may exacerbate disease. We compared Tc HMPAO labelled white cells, plain films and air insufflation in 10 patients with biopsy proven ulcerative colitis who presented in severe exacerbation of symptoms. All examinations were performed on the same day. In eight, the extent of disease as assessed by white cell scanning correlated exactly with air enema. In all but one, the plain abdominal film severely underestimated disease. In the remaining two cases, all investigations were normal and the disease activity had subsided by the time the studies were performed. All 10 patients found the radionuclide study preferable to the air enema. In conclusion, white cell scanning provides an alternative, safer and less invasive means of assessing the extent of disease in the acute exacerbation of IBD, with greater patient tolerance.

Barium meal diagnosis of coeliac disease

S. J. Armstrong and J. Virjee
Department of Radiodiagnosis, Bristol Royal Infirmary, Bristol BS2 8HW, UK

The features of coeliac disease on small bowel follow-through or enema are well described, however, many patients with undiagnosed coeliac disease present with symptoms of vague epigastric pain or discomfort and are initially referred for a barium meal rather than a small bowel examination. We describe two signs which, if present on a barium meal either alone, or particulary in combination, will alert the radiologist to a diagnosis of coeliac disease. The first is the loss of valvulae conniventes in the duodenum resulting in a "bald" or featureless duodenum. This can be observed in several other conditions but is particularly suggestive of coeliac disease if the featureless appearance extends into the fourth part of the duodenum or proximal jejunum. The second sign is the presence of gastric metaplasia involving the second part of the duodenum. In 10 patients referred from either GPs or hospital outpatients with non-specific symptoms of epigastric discomfort, diarrhoea, weight loss or anaemia, a diagnosis of coeliac disease was suggested by the presence of one or both of the above signs on barium meal examination. In each case the diagnosis was subsequently confirmed by jejunal biopsy.

Abdominal ultrasound as the primary diagnostic procedure in patients with suspected small bowel Crohn's disease

D.A. Nicholson, M. B. Sheridan and D. F. Martin
Department of Radiology, Withington Hospital, University Hospital of South Manchester, Manchester M20 8LR, UK

The need to exclude small intestinal inflammatory bowel disease is a common cause of referral for small bowel barium examination. Despite attempts to select patients on clinical grounds, the majority of small bowel barium examinations will be normal. In order to allow more selective use of barium examination and to minimize radiation exposure, we have evaluated the use of transabdominal ultrasound examination of the small bowel prior to barium examination in all patients referred with the clinical suspicion of small intestinal Crohn's disease. To date, 57 patients (33 female, 24 male, age range 18 – 84 years, mean 43) have been examined immediately prior to barium examination performed by a different radiologist, unaware of the ultrasound findings. Ten of 12 patients with active Crohn's disease have been correctly identified, as have 44 of 45 patients without disease. The two false-negative investigations occurred during the early part of our experience. These results support the use of abdominal ultrasound as a procedure which can select appropriate patients for small bowel barium examination and minimize radiation exposure in patients who do not harbour disease.

Defaecating videoproctography following restorative proctocolectomy

M. McNicholas, M. Logan, J. Masterson and *J. Hyland
*Departments of Radiology and *Surgery, St Vincent's Hospital, Dublin 4, Ireland*

Defaecating video proctography is an accepted method for the investigation of patients with problems of defaecation and a range of measureable parameters has been established. Restorative proctocolectomy is now the procedure of choice in selected patients undergoing elective surgery for ulcerative colitis. We wished to study the mechanism of pouch emptying in these patients and to define the range of radiological appearances of the normal ileal pouch. We have attempted to identify the measureable parameters which are of use in this group by correlation with clinical outcome and manometric studies. Fourteen patients were studied, mean age 35 years, mean interval since surgery 35 months. Ano-pouch angle, pelvic floor descent, anal opening, pouch anatomy and dynamics of pouch emptying were assessed. The ano-pouch angle varied widely and did not correlate with function. Excessive pelvic floor descent was associated with inervation damage of the pelvic floor. Poor anal opening was associated with anastemotic stricture. The radiological appearances of the pouches varied widely. No coordinated pouch peristalsis was seen and all patients emptied their pouches by increasing their intra-abdominal pressure. The importance of a post evacuation film to assess adequacy of emptying is stressed.

Balloon dilatation of anastomotic rectal strictures

K. D. McBride, *J. Geraghty, *J. J. Murphy, *D. Campbell and D. P. MacErlean
*Departments of Diagnostic Imaging and *Surgery, St Vincent's Hospital, Elm Park, Dublin 4, Ireland*

Rectal stricture has been a difficult complication to manage after anterior resection, traditionally with metal dilators or resection. A technique, using fluoroscopically controlled balloon dilatation for benign anastomotic rectal strictures, is presented. Eight patients are included, seven females and one male, with a mean age of 63 years. The original diagnosis was rectal malignancy in four, and diverticular disease in four. Six patients had a stapled anastomosis. Four patients required a single dilatation and the remainder a mean of three dilatations. The mean diameter of the stricture increased from 7.2 mm pre-dilatation to 17.0 mm after the last dilatation. Symptomatic relief was achieved in all cases without any complications. Balloon dilatation of the rectum is safe and effective and should be considered as the treatment of choice for benign anastomotic rectal strictures.

Gastrointestinal lumenal cytology: a radiological procedure

S. J. Morris and J. Virjee
Department of Radiodiagnosis, Bristol Royal Infirmary, Bristol BS2 8HW, UK

Cytological specimens can easily be obtained by the radiologist from oesophageal, gastric, duodenal and rectal lesions at the time of the initial barium investigation, thus obviating the need for a second hospital visit for endoscopy, proctoscopy or sigmoidoscopy and biopsy, the first of which is costly, time-consuming and requires sedation and nursing assistance. Specimens have been obtained from 41 lesions in the upper and lower gastrointestinal tract using a disposable Wilson—Cook cytology brush. For oesophageal and gastric lesions the patient swallows the plastic sleeve containing the brush with a sip of barium to outline the lesion, the tip is screened into position and specimens obtained. No local anaesthesia is required. For duodenal lesions the brush is passed through a Bilbao—Dotter tube and for rectal lesions it is introduced via the Miller rectal tube. Cytological results have been confirmed by endoscopy and biopsy, surgical or post-mortem histology, with a high true positive rate and a false negative rate comparable with endoscopy. The procedure is simple and quick, effective dose equivalent measured by thermoluminescent dosemeters is very low, no local anaesthesia is required, no complications have been encountered and patient acceptability is high.

The role of angiography in the assessment of patients with acute or chronic gastrointestinal haemorrhage

S. C. Whitaker and R. H. Gregson
Department of Radiology, University Hospital, Nottingham NG7 2UH, UK

We have reviewed the case notes, angiograms and pathological data of all patients with a clinical diagnosis of gastrointestinal bleeding who underwent visceral angiography during the 8 year period between January 1983 and December 1990. Over 60 patients were referred, 42% female and 52% male. Approximately 80% of patients had an acute history of bleeding and 20% had a chronic history of anaemia (with or without a previous history of gastrointestinal bleeding). Other relevant clinical information, including the number and variety of investigations undertaken prior to angiography, has been analysed and is presented. All patients except three had selective coeliac and mesenteric angiography. Nineteen angiograms showed no abnormality and the remainder showed either a vascular abnormality or evidence of active bleeding. One patient had an aortogram only and in two patients angiography was considered a technical failure. In those patients that presented acutely, 75% of angiograms were requested urgently and the rest were performed as elective procedures. In as many cases as possible, clinical follow-up has been obtained and the true diagnosis determined from surgical or pathological data. The role of angiography in the assessment of patients with gastrointestinal haemorrhage is discussed in the light of these results.

The final outcome in gastrointestinal haemorrhage following normal mesenteric angiography

D. Kinsella, J. Kabala and J. Virjee
Department of Radiodiagnosis, Bristol Royal Infirmary, Bristol BS2 8HW, UK

Selective mesenteric angiography is an established technique in the investigation of gastrointestinal bleeding. A total of 35 patients underwent this investigation over a 4 year period at the Bristol Royal Infirmary. The results of the angiograms were analysed retrospectively along with the results of upper and lower gastrointestinal endoscopy, contrast studies and nuclear medicine scans. The pick-up rate of angiography in patients with different presentations and transfusion requirements is presented. Also, the characteristics of patients with gastrointestinal haemorrhage but normal angiography and other investigations are discussed with particular reference to their final outcome.

Detection of unsuspected lesions other than gall bladder pathology during cholecystosonography

B. Banerjee and B. R. Choraria
Department of Radiodiagnosis, Tameside General Hospital, Ashton-under-Lyne OL6 9RW, UK

One of the distinct advantages of cholecystosonography over the conventional cholecystography, is the ability of the ultrasound to detect clinically unsuspected lesions of the surrounding organs without the need for further preparation of patients, use of contrast agents, or radiation. One thousand and fifty patients referred by clinicians to the radiology department solely for the investigation of gall bladder and biliary tract were included in the series. Sonography was performed with real time ultrasound machines using 3.5 MHz and 5 MHz probes. The gall bladder and biliary tract were examined initially, following which a rapid sonographic survey of the rest of the abdomen was undertaken. In a sample group of 100 patients, selected at random, the times required to scan the gall bladder and to scan the rest of the abdomen were separately recorded. Additional time required to perform sonography of the rest of the abdomen was on average 3.5 minutes. Abnormalities other than gall bladder pathology were noted in 123 patients but in 47 patients the lesions were considered clinically significant which required active management. In seven patients in this group, gall stones were also present. We therefore conclude that examination of the whole of the abdomen during cholecystosonography is a prudent policy.

Herniation of the large bowel through the diaphragmatic oesophageal hiatus

P. A. J Tesar and J. Virjee
Department of Radiodiagnosis, Bristol Royal Infirmary, Bristol, UK

Conventional teaching states that in adults, the large bowel herniates through the diaphragm either via Bochdalek or Morgagni foramina or via a post-traumatic diaphragmatic tear. Thirteen adults were found on barium enema examination to have large bowel located above the diaphragm and barium meal studies were done on all of them. These studies showed the presence of hiatus hernia in all, the intimate relationship of colon and herniated stomach in all, and volvulus of the stomach in the majority. It is concluded that the conventional teaching should be revised. In adults the colon usually herniates through the oesophageal diaphragmatic hiatus, not the foramina or Morgagni or Bochdalek. It is often associated with a large unrecognized gastric hernia and volvulus.

Prompt radiological diagnosis of retroperitoneal perforation following therapeutic ERCP is important in determining the outcome of treatment

D. F. Martin
Department of Radiology, Withington Hospital, University Hospital of South Manchester, Manchester M20 8LR, UK

Retroperitoneal perforation is a rare complication of therapeutic ERCP (endoscopic sphinterotomy, endoprosthesis insertion) reportedly occurring in 0.1%. Controversy exists regarding management, conservative measures failing mainly because diagnosis is delayed until the patient is symptomatic, surgery then proving necessary for drainage and repair. A policy of scrutinizing a supine upper abdominal film taken at the completion of the procedure in all patients has been evaluated. Retroperitoneal perforation was detected by the presence of air or contrast medium in any retroperitoneal compartment. Fourteen patients with retroperitoneal perforation have been identified. Air or contrast was evident in the anterior pararenal space (nine), right perinephric space (nine) or posterior pararenal space (one). All perforations were evident at the time of examination, no patient with retroperitoneal perforation has been identified after leaving the Department. Conservative therapy with nasogastric suction, intravenous fluids and antibiotics as well as the provision of adequate biliary drainage was successful in all patients. Only three of 14 patients became symptomatic and no interventional procedure was necessary. Early detection of retroperitoneal perforation and prompt institution of conservative measures can be expected to be successful.

The value of ultrasound examination in patients undergoing ERCP for suspected biliary and pancreatic disease

J. M. E. Kirk, J. E. Stutley, C. Sampson, M. J. Knight and A. E. A. J. Joseph
Department of Diagnostic Radiology, St George's Hospital, London SW17 0QT, UK

To assess the value of ultrasound examination performed immediately prior to ERCP, the results of 214 examinations were analysed prospectively. Ten ultrasound and 51 ERCP examinations were incomplete. Of the 153 adequate examinations, ERCP and ultrasound agreed in 114 (74.5%). Both examinations agreed in 76.7% of common bile duct calculi, 80% of pancreatitis and 93.4% of tumours. ERCP alone diagnosed common bile duct calculi in 10 examinations. In five, ultrasound of the biliary tree was reported as normal, but in four of these the common bile duct was not dilated on either examination: in one a calculus was misinterpreted as pancreatic mass. The fifth ultrasound examination, on review, was inadequate. ERCP diagnosed pancreatic lesions in two ultrasonically normal examinations but in one, computed tomography did not confirm the ERCP diagnosis of chronic pancreatitis and the other, diagnosed at ERCP as a pancreatic tumour, histologically was chronic pancreatitis. Ultrasound correctly diagnosed a cholangiocarcinoma not seen on ERCP. Our results show that 42 ERCP examinations would have been avoided if ERCP had not been done where ultrasound was normal, but five common bile duct calculi would have been missed and one case of pancreatitis. We recommend that the decision to perform ERCP should be carefully reconsidered where the ultrasound examination is normal.

2.30 - 3.45

Musculoskeletal Imaging

Clarence Room

Cross sectional imaging of the shoulder joint

P.E. Peters, Th. Vestring and G. Bongartz
Department of Clinical Radiology, University of Münster, Albert-Schweitzer-Str.33, 4400 Münster, Germany

In this presentation the current techniques and indications for computed tomography (CT) and magnetic resonance imaging (MRI) of the shoulder joint are discussed. Ultrasonography (US), although a cross sectional imaging technique will be only mentioned in the context of comparative studies. Magnetic resonance imaging of the shoulder joint has been accepted surprisingly rapidly by the referring physicians. At our institution, 28% of all MRI studies concern the musculo-skeletal system. From this subgroup, 12% are shoulder joint examinations. Thus, in MRI of joints, the shoulder ranges second only to the knee joint. From a technical viewpoint MRI of the shoulder joint suffers from the anatomical drawback of being located will outside the central axis of the human body. However, by means of off-centre zoom and specially designed surface coils, a consistently high image quality can be obtained. The imaging plane is usually selected according to the suspected clinical problem. The most useful projections include coronal and sagittal obliques and transaxial views. Both T_1- and T_2-weighted spin-echo and gradient-echo techniques are applied. The latter mainly as FLASH 20 sequence which is best suited to detect pathologic changes of the labrum glenoidale. Suspected rotator cuff pathology and/or impingement syndrome are the most common causes for referral. A score system has been developed for the diagnosis of impingement syndrome in patients with painful shoulder. Owing to the large range of motion, the shoulder joint is the most commonly dislocated joint in the body. The diagnosis of shoulder instability used to be a clear domaine of CT combined with double contrast arthrography. However, since MRI non-invasively depicts the bony defects as well as the labrum glenoidale, the number of CT studies has decreased markedly.

Follow-up magnetic resonance imaging examinations in rheumatoid arthritis

A. Mundinger, E. Dinkel, A. Beck, S. Meske and G. Sigmund
Department of Radiology, University Clinics, Hugstetter Strasse 55, 7800 Freiburg, FRG

The diagnostic value of magnetic resonance imaging (MRI) in patients with rheumatoid arthritis has been emphasized. However, there are only few follow-up data concerning MRI changes in these patients. In 46 patients with rheumatoid arthritis, a total of 137 MRI examinations of the hand and knee as well as of other joints was obtained at 0.23 T or 2 T. The follow-up interval ranged from 3 to 28 months (average 10 months). The study protocol included T1- and T2-weighted spin—echo, in some cases additional RARE and gradient-echo sequences. The arthritis was classified as follows: exudative, effusions present; proliferative, synovial hypertrophy or pannus formation; destructive, presence of erosions. The typical feature of rheumatoid arthritis was a combination of the proliferative and the destructive types. A progression of MRI changes was seen in 18 of the 46 patients. The localization and extent of pannus was taken into account for synovectomy. Regression of effusions or reduced activity of pannus were noted in 11 patients. No substantial changes occurred in 10 patients. In conclusion, the follow-up of MRI changes reflected the aggressive course of rheumatoid arthritis. Monitoring of intra-articular soft tissue and osseous changes by MRI can substantially contribute to therapeutic decisions.

Nott's disease: an atypical erosive arthritis of the hands

M. J. Cobby, *J. Cushnahan, *P. A. Dieppe and I. Watt
*Departments of Radiology and *Rheumatology, Bristol Royal Infirmary, Bristol BS2 8HW, UK*

Osteoarthritis may result from, or coexist with rheumatoid arthritis (RA). In addition erosive osteoarthritis (EOA) has been associated with connective tissue disorders such as the Sicca syndrome. In this series, five patients with an atypical form of erosive arthritis are described who demonstrated features of both EOA and RA. Five patients, four female and one male, with a mean age of 58 years, showed an unusual combination of radiological findings with typical features of interphalangeal EOA and non-proliferative marginal erosions in the wrists. Serial radiographs of the hands, wrists and other symptomatic joints were reviewed, together with the clinical findings and serological investigations. Follow-up ranged from 1 to 5 years. All patients were seronegative for rheumatoid and anti-nuclear factors and none had any of the systemic features of RA, Sicca syndrome or any other connective tissue disease. Involvement outside the hands was confined to changes in the elbow, hip and cervical spine in one patient each and RA-like erosions of the foot in two cases. The EOA changes in the fingers and RA-like changes in the wrists evolved concurrently, suggesting that these patients did not have two separate disorders. "Nott's disease" may represent an overlap syndrome, resulting in an arthropathy with features of both EOA and RA.

Angiographic changes in the neuropathic foot

B. P. Menanteau, C. Marcus, V. Ladam, A. Lepreux and F. Gausserand
Department of Radiology, Robert Debré Hospital, University of Reims, 51092 Reims Cedex, France

The pathogenesis of the neurotrophic joint has long been a subject of controversy between the neurotraumatic versus neurovascular theories. To gain better understanding of the pathogenesis, we studied the distal circulation in patients presenting with neuropathic foot. Angiographies of 32 patients with neuroarthropathy of the foot were reviewed, including seven diabetic patients. Both lower extremities were studied by retrograde femoral puncture. Specific anteroposterior and lateral views were obtained with attention to the particular joint affected, the type of changes present, and the time sequence involved. We also measured the blood flow velocity. In 28 patients with destructive or acute joint, we found hyperaemia surrounding the affected joint and significant increases in blood flow, associated with arteriovenous shunting in the neuropathic limb. However, vascularity was found to be quite normal in patients with hypertrophic or chronic joint. The angiographic data of this series strongly support the validity of the neurovascular theory which states that the changes result from a neurally initiated reflex that leads to very active resorption by osteoclasts in an area supplied by a particular vascular bed.

Does the metacarpal index have a place in making the diagnosis of Marfans syndrome?

K. A. Younger, A. Child and A. G. Wilson
Department of Diagnostic Radiology, St George's Hospital, London SW17 0QT, UK

This study was undertaken to assess the importance of the metacarpal index (MCI) in making a diagnosis of Marfans syndrome and to assess in particular whether it could be replaced by simple clinical measurements such as arm span, upper/lower segment ratio or hand/finger ratio. Hand radiographs were obtained in 40 Caucasian adults with Marfans syndrome. Height, arm span, upper/lower segment, hand and finger lengths were measured in these subjects. Sex, handedness, eye and cardiac findings were also noted. The control group comprised Caucasian adult accident and emergency patients excluding those with injuries to the metacarpals. Sex, handedness and height were documented in these. The influence of gender, handedness and height on the MCI was assessed. Preliminary data suggest that simple clinical measurements of the patient provide the same information as the MCI, without the use of ionizing radiation.

Magnetic resonance imaging in dialysis-related amyloid arthropathy

M. J. Cobby, R. S. Adler, *R. Swartz and W. Martel
*Departments of Radiology and *Nephrology, University of Michigan Medical Center, Ann Arbor, MI 48109, USA*

Dialysis-related amyloidosis (DRA) is a recently recognized complication of long-term haemodialysis due to the deposition of a unique form of amyloid derived from circulating beta 2-microglobulin. It is characterized by painful stiff joints. The carpal tunnel syndrome is a common presentation. This study documents the magnetic resonance (MR) characterisitcs of DRA in six articular sites of five patients. All patients had been on maintenance haemodialysis for 8 years or more and had biopsy proven, or clinically and radiologically suspected amyloidosis. Three wrists, a shoulder, knee and thoracic spine were examined. The extent of osseous and soft tissue involvement at each site was well demonstrated. A number of lesions that were apparently intraosseous on conventional radiographs were shown to be due to well defined articular surface erosions on MR imaging. The amyloid deposits were of intermediate to low signal intensity on all sequences. Synovial involvement was associated with joint effusions. Fat suppression techniques enhanced visualization of intraosseous deposits. This study has shown that MR imaging is well suited to demonstrating the extent and distribution of involvement in DRA. The signal characteristics of amyloid infiltration distinguish it from cellular or high water containing lesions such as inflammatory masses, acute or chronic synovitis and Brown tumours of hyperparathyroidism.

Evaluation of osseous lesions of the lower limb by magnetic resonance imaging

J. M. Hawnaur, J. P. R. Jenkins and I. Isherwood
Department of Diagnostic Radiology, University of Manchester, Manchester M13 9PT, UK

The aim of the study was to assess the ability of magnetic resonance imaging (MRI) to characterize bony abnormalities of the tibia and fibula compared with conventional radiography and computed tomography (CT). Twenty patients (nine male, 11 female, aged 8–61 years) with clinical and plain film evidence of a bone lesion in the lower limb were reviewed. Magnetic resonance imaging was performed at 0.26 T using spin echo (SE 560–1500/26–80) and partial saturation recovery (PSR 500/18) sequences in multiple planes. Gadolinium-DTPA (Gd-DTPA) was given intravenously in seven patients. A retrospective study was made of MR, CT and clinicopathological findings. There was good concordance between MRI and CT regarding separation of benign from malignant tumours and neoplastic from non-neoplastic pathologies. Cortical thickening associated with some benign tumours, chronic osteomyelitis and stress fracture were identified as widening of the low signal intensity cortex on all MR sequences. Alteration of signal was observed as a result of marrow oedema and periosteal reaction enabling differentiation of active from inactive disease. Cortical soft tissue foci and permeation by infection or malignancy were detected on T_2- or Gd-DTPA enhanced T_1- weighted MR images as relatively hyperintense areas, whilst sclerosis or dense calcification resulted in low signal intensity. More subtle calcification could not always be demonstrated on MRI. Extraosseous soft tissue extension, lesion extent and relationship to joints were better appreciated on longitudinally orientated MR scans than on transverse CT. Magnetic resonance imaging with a plain radiograph provided similar or superior diagnostic information to CT in bony lesions of the tibia and fibula.

Bone cortical and periosteal changes as seen on magnetic resonance imaging

G. B. Greenfield
Department of Radiology and Diagnostic Imaging, H. Lee Moffitt Cancer Center and Research Institute, P. O. Box 280179, Tampa, FL 33682-0179, USA

Magnetic resonance imaging (MRI) is now widely accepted as a means of demonstrating bone marrow and soft tissue detail. Its ability to elucidate bony changes has been less well appreciated. The basic changes of cortical destruction with geographic or permeative destructive patterns, and erosion of the cortex can also be demonstrated. In some cases, cortical destruction can be better shown on MRI than on conventional films. The patterns of periosteal reaction, including simple periosteal reaction, spiculated periosteal reaction, and laminated or "onion-skin" periosteal reaction can be well seen. The cortex is seen as a solid black line and interruptions of the cortex can be seen as high signal intensity on proton density and on T2 weighted images. The various changes on MRI are illustrated and compared with conventional radiographs and computed tomography.

The incidence and significance of fluid/fluid levels on computed tomography of osseous lesions

A. M. Davies, V. N. Cassar-Pullicino, V. Goswami and R. J. Grimer
Radiology and Bone Tumour Treatment Services, Royal Orthopaedic Hospital, Birmingham B31 2AP, UK

The demonstration of a fluid/fluid level (FFL) within an osseous lesion on computed tomography (CT) has been reported as suggestive of an aneurysmal bone cyst (ABC) although FFLs have also been rarely found in association with other pathologies. This study was conducted to determine the frequency of FFLs on CT on a series of patients presenting to a major tertiary referral centre for the treatment of bone tumours. In the 34 months study period, 14 ABCs were found out of 447 bone "tumours" referred. Computed tomography of the ABCs revealed FFLs in 12 (85.7%) cases. Within the same period, 673 CTs of bone lesions were performed and FFLs identified in two further cases: a massive telangiectatic osteosarcoma and a conventional osteosarcoma following chemotherapy. In quantitative terms the significance of an FFL on CT as being diagnostic of an ABC is as follows: sensitivity, 85.7%; specificity, 99.7%; positive predictive value, 85.7%; negative predictive value, 99.7%; accuracy, 99.4%. An FFL within a bone lesion on CT remains strongly suggestive of an ABC although the radiologist should be wary of a rare telangiectatic osteosarcoma. A further nine ABCs, with CT, outside the study period or from elsewhere, were added to the original cases. An FFL was present in 19 (82.6%) cases, multiple in 15. Fluid/fluid levels are typical of the mid ("blow-out") or late phase of the development of an ABC and not the incipient ("permeative") stage or where the internal architecture of the tumour has been disrupted by biopsy or previous surgery.

Magnetic resonance imaging of desmoid tumours

J. Kabala and P. Goddard
Bristol Magnetic Resonance Imaging Centre, Frenchay Hospital, Bristol BS2 8HW, UK

Desmoid tumours are benign infiltrating fibromatous lesions. Their extent and nature can be difficult to determine on computed tomography. Nine magnetic resonance scans were performed on four patients (three female, one male, ages 8–35) with desmoid tumours (two thoracic, two pelvic) providing excellent delineation of the lesions. Initial scans showed well defined masses with the following signal intensities: T_1 weighted sequence, predominantly homogenous medium intensity containing small areas of irregular very low signal, three patients showed an apparent low signal capsule; short tau inversion recovery, homogeneous high signal intensity containing small areas of very low signal; T_2 weighted, heterogenous pattern of high and very high signal containing small areas of very low signal. One patient 11 months after radiotherapy showed progressive increase in the size of the very low signal intensity areas which became the predominant appearance by 38 months. Another patient, not similarly treated, showed no change in signal after 18 months. It is suggested that the low intensity areas represent relatively inactive dehydrated fibrous tissue.

CENTRAL LIBRARY

2.30 – 3.45

Radiotherapy For Pelvic Tumours

Balmoral Room

The place for radiotherapy in the primary management of prostate cancer

D. P Dearnaley
Academic Unit, Department of Radiotherapy and Oncology, The Royal Marsden Hospital and Institute of Cancer Research, Downs Road, Sutton, Surrey SM2 5PT, UK

Prostate cancer ranks third in incidence of the malignancies occurring in men. In the UK, approximately 8000 cases of prostate cancer are registered per year with 6000 men dying annually with disease. Curative therapy is only possible in the cohort with localized tumours; an estimate of the size of this sub-population shows a wide variation from 10% in some UK series to 57% in the USA. How should early localized prostate cancer be managed? The options include radical prostatectomy, radical radiotherapy or "surveillance", a policy suitable for an elderly population with a cancer with a slowly evolving natural history and many competing causes of death. Adequate comparison of these alternatives has yet to be undertaken but has become of increasing importance with attempts to screen for early disease. How can we optimize results using radiotherapy? Local control is improved for bulky tumours by increasing the dose to 70 Gy, but at the cost of an increased incidence of radiation-induced complications. There is no evidence to support elective lymph node irradiation but irradiation complications increase with larger field sizes. Initial enthusiasm for interstitial irradiation has not stood the test of time, and neutron therapy remains to be fully evaluated. Combination therapy with androgen deprivation and radiotherapy may improve the therapeutic ratio and is being assessed in prospective randomized studies.

Computerized image analysis in prostatic neoplasia

P. D. Miller, C. Sowter, G. Slavin and R. S. Kirby
Department of Urology, St Bartholomew's Hospital, London EC1A 7BE, UK

There is good evidence that interaction between glandular epithelium and stromal components in prostatic tissue plays a critical role in the pathogenesis of benign prostatic hyperplasia (BPH). This may be mediated by soluble growth factors such as the epidermal growth factor (EGF), which has been identified in BPH tissue, and its receptors can be assayed. Immunohistochemical studies have shown that EGF receptors are confined to the glandular epithelium. The IBAS image array processor can be used to quantify automatically glandular and stromal tissue components in each field of a histological section. Tissue was obtained by transurethral resection from 30 patients with BPH. The relative amounts of the tissue components (epithelium, lumen and stroma) were measured in each field, and a mean value of a representative number of fields was compared with the values obtained for EGF binding by radioligand assay. Our results show that although BPH is mainly a stromal disease, there is a wide variation in the proportion of glandular tissue between glands (range 10.5–41.2%). Low levels of EGF binding were found in those specimens where there was little glandular hyperplasia. We believe that this technique, when applied to other biochemical parameters, will help us to understand stromal–epithelial interactions in the pathogenesis of BPH and prostatic carcinoma.

Total cystectomy and substitution enterocystoplasty – an alternative primary treatment for stage T2/3 bladder carcinoma

S. A. V. Holmes, T. J. Christmas, R. S. Kirby and W. F. Hendry
Department of Urology, St Bartholomew's Hospital, London EC1A 7BE, UK

In the UK, the current treatment for stage T2/3 bladder carcinoma is total cystectomy and urinary diversion or external beam radiotherapy (EBRT) with or without salvage cystectomy. Unfortunately, EBRT precludes subsequent enterocystoplasty owing to radiation enteritis, and conventional total cystectomy inevitably causes erectile impotence as well as a disagreeable stoma. We have performed nerve-sparing total cystectomy and enterocystoplasty as primary treatment for bladder carcinoma in 11 cases (two female, nine male) of mean age 49 (range 24–64) years. The bladder was reconstructed with ileum (n=4), caecum (n=2) or ileum and caecum (n=5) without mortality or significant morbidity. Post-operatively, all were continent and 50% had full erectile potency. The mean follow-up is 28 months; three (27%) have developed recurrent disease, one of which required local EBRT and urinary diversion. Nerve-sparing cystectomy and cystoplasty is an attractive alternative to EBRT in bladder carcinoma. The preservation of potency and lack of a stoma or EBRT side-effects are an advantage, and the short-term results are encouraging.

The post-irradiation bladder: a functional model

J. A. Vale, H. N. Whitfield and K. R. Trott
Departments of Urology and Radiation Biology,
St Bartholomew's Hospital, London EC1, UK

Radiotherapy is still the treatment of choice for locally invasive bladder carcinoma in the UK. However, subsequent changes in bladder function are a cause of morbidity in up to 50% of patients. We have developed a small animal model for the further study of this troublesome complication. Young adult female Wistar rats (180–220g) were irradiated with X-rays at doses of 15, 20 and 25 Gy. Subsequently, cystometry was performed weekly: anaesthesia was achieved using enflurane in nitrous oxide and oxygen, and a ureteric catheter (3–5 Ch.) was introduced per urethra. The bladder was emptied by digital pressure, and slow-fill cystometry was performed using sterile water delivered by a syringe driver at a rate of 0.05 ml/min. Intravesical pressure was monitored by a pressure transducer connected to a specially designed evaluation box and chart recorder. The volume infused to produce a pressure rise of 5 cm of water was taken as an index of compliance. A biphasic reduction in compliance was demonstrated. The first reduction occurred at about 4 weeks and was proportional to the radiation dose: it reached 40% in the 25 Gy group. After transient recovery, a second irreversible reduction started at 3–4 months; compliance was reduced by 35% in the 15 Gy group, 40% in the 20 Gy group, and 50% in the 25 Gy group.

Prostate-specific antigen in monitoring prostatic carcinoma

P. D. Miller, J. Vale and R. S. Kirby
Department of Urology, St Bartholomew's Hospital,
London EC1A 7BE, UK

In excess of 75% of patients with carcinoma of the prostate have disseminated disease on presentation, although they may not have metastatic symptoms. It has been traditional to perform a bone scan after a tissue diagnosis has been made, and many patients are monitored with serial bone scans. We have assessed 78 patients with histologically proven carcinoma of the prostate with prostate-specific antigen (PSA) and bone scan on initial presentation and subsequent follow-up over 2 years. A Hybritech Tandem PSA-R assay was used for all serum PSA measurements and a whole body bone scan was performed and reported by an experienced radiologist. Of 31 patients who had a positive bone scan at presentation, four patients (13%) had a PSA less than 10 ng/ml. In those who had consistently negative bone scans (n=34), six (17.6%) had a PSA greater than 10 ng/ml, but only two (5.8%) were greater than 30 ng/ml. In the patients who became bone scan positive during this period (n=13), all had an earlier rise in PSA and ultimate values greater than 200 ng/ml. PSA is a sensitive marker that has been shown to enhance assessment of disease bulk and control in prostatic cancer. False negative PSAs may occur and are probably due to tumour dedifferentiation, while false positives are often due to concomitant benign hyperplasia. We conclude that the serial bone scans may be avoided when monitoring disease progression but they cannot at present be replaced by PSA in the initial staging of prostatic carcinoma.

Radical prostatectomy – the treatment of choice for stage T1/2 carcinoma of the prostate?

T. J. Christmas, P. D. Miller and R. S. Kirby
Department of Urology, St Bartholomew's Hospital,
London EC1A 4BE, UK

In the UK, stage T1/2 carcinoma of the prostate may be treated by radiotherapy (RT), hormonal manipulation or expectant policy. Radical supra-pubic prostatectomy is the treatment of choice for such cases in the USA. We have operated on a consecutive series of 11 cases with clinical stage T0–2 carcinoma of the prostate, of mean age 66 years (range 52–79), assessed by prostate-specific antigen (PSA), trans-rectal ultrasound with biopsy, pelvic computed tomography scan and isotope bone scan. The PSA was less than 30 ng/ml in each case. A frozen section of iliac lymphadenectomy specimens was negative in eight cases; each then underwent nerve-sparing radical prostatectomy, and positive cases had bilateral orchidectomy. Histology confirmed stage T0–2 in seven cases, the T3 patient was treated later with external beam RT. There was no mortality and the mean follow-up time is 16 months (range 3–30). In all eight cases, the PSA has remained less than 2 ng/ml. One case developed anastomotic stricture requiring endoscopic resection. Erectile potency has been preserved in 50%. Although the long-term results of radical prostatectomy compared with RT are awaited, this procedure offers a potential cure for prostatic carcinoma without significant morbidity.

Growth control in prostatic neoplasia

P. D. Miller, S. Liu and R. S Kirby
Department of Urology. St Bartholomew's Hospital,
London EC1A 7BE, UK

There are distinct zones within the prostate and the majority of cancers arise in the peripheral zone, whereas prostatic hyperplasia (BPH) originates in the periurethral transitional zone. This study aimed to compare epidermal growth factor receptor (EGFR) binding these zones, and between BPH and prostatic cancer. Specimens were taken with ultrasound guided biopsy in patients with BPH (n=25), carcinoma (n=12) and controls (n=12). Epidermal growth factor receptor binding was measured with a single-dose binding assay, and full Scatchard analysis when sufficient tissue was obtained at subsequent operation. In the patients with BPH, a significantly greater concentration of specific EGF binding was found in the transitional zone (75.7±5.14 fmol/mg protein) compared with the peripheral zone (19.4±2.3), and the biphasic Scatchard plots suggested two different receptor binding affinities in BPH tissue. There was increased specific binding in the prostatic carcinomas (137.9±28.2), compared with the controls (44.1±6.3), this was associated with loss of the low affinity binding site. In the control group the difference between the two zones was less marked. These results suggest that EGF is involved not only in the pathogenesis of BPH but also in the proliferation of prostatic cancer cells. Furthermore, the developing imbalance of high and low affinity sites may be associated with tumour dedifferentiation.

Maximizing local control by customized dose prescription for pelvic tumours

A. E. Nahum and *D. M. Tait
*Joint Department of Physics and *Radiotherapy, Royal Marsden Hospital, Sutton, Surrey SM2 5PT, UK*

Pelvic malignancies exhibit steep dose–response curves and hence offer scope for improved local control. Normally, it is assumed that the target dose can only be increased by better conformation of the radiation field to the shape of the target. However, dose–volume histograms (DVHs) calculated from three-dimensional distributions in organs at risk, such as the rectum, reveal considerable interpatient variability even for standardized plans. We have retrospectively analysed the rectal DVHs for 100 pelvic plans and computed complication probabilities for late rectal damage (RCP) according to the recent Kutcher–Burman model (Kutcher & Burman, 1989), choosing parameters consistent with clinical expectations. In the cases where the predicted RCP was very low, the target dose was increased until the RCP reached an "acceptable" 5%. We show that the resultant increase in tumour control probability (TCP), predicted from a simple model of cell killing, is substantial in a significant fraction of the patients. This study thus indicates that local control in the pelvis can be significantly increased if the tumour dose prescription is individualized on the basis of three-dimensional dose distributions in organs at risk.

Reference

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Reduction in adverse radiation effect by a simple conformational technique in radiotherapy for early carcinoma of the prostate

G. Read, D. Mott and J. Wilkinson
Departments of Radiotherapy and Physics, Christie Hospital and Holt Radium Institute, Withington, Manchester M20 9BX, UK

Radiotherapy for early prostate cancer is frequently compromised by the unavoidable inclusion of part of the rectum in the field. A simple conformational technique has been devised which enables shielding of the rectum to be introduced. Computed tomography of the prostate is employed and the target area chosen on each slice. A modification of the radiotherapy plan system is employed to set up a four-field arrangement of fields of suitable size and a program enables the production of templates scaled to fit the lead block trays. Using a standard dose and fractionation (target dose 50 Gy in 16 fractions over 21 days), adverse radiation effects were recorded in 93 patients with T2–T4 N0 M0 carcinoma of the prostate treated with the new conformational technique and compared with 152 patients who had received the previous standard rotation technique. A significant reduction in the severity of the rectal reaction as assessed by WHO scoring was found. In particular, five patients required surgical intervention for rectal necrosis in the rotation group compared with none treated with the conformational technique.

The management of ureteric stricture following external beam radiotherapy and Wertheim's hysterectomy for cervical carcinoma

T. J. Christmas, J. A. Vale and W. F. Hendry
Department of Urology, St Bartholomew's Hospital, London EC1A 4BE, UK

Radical pelvic surgery and radiotherapy (RT) can lead to impairment of the blood supply to the distal ureter; a combination of the two may lead to ischaemic stricture. We have treated eight women, of mean age 42 years, following curative Wertheim's hysterectomy and adjuvant RT for cervical carcinoma, in whom unilateral distal ureteric stricture occurred. Seven presented with loin pain, one with urinary tract infection secondary to obstruction. The initial treatment was percutaneous nephrostomy in two and internal drainage by J-J stent in six. One developed pyonephrosis, with a J-J stent *in situ*, necessitating nephrectomy. Reconstructive surgical options include bladder psoas hitch with ureteric reimplantation, appendiceal or ileal interposition and transuretero-ureterostomy. The importance of early recognition and short- and long-term management of ureteric stricture following RT, as well as the timing and choice of surgical intervention, are discussed.

2.30 – 3.45

Radiosurgery

Lancaster Room

Ultrasound surgery; a review

G. ter Haar
Physics Department, The Royal Marsden Hospital, Sutton, Surrey SM2 5PT, UK

Ultrasound is unique among the other forms of radiation commonly used in medicine in that it can be tightly focused within the body. This allows the possibility that when high powers are used, the high intensity developed within the focal region may be used to produce highly localized tissue damage at depth, without harm to overlying structures. This technique is known as ultrasound focal surgery. Ultrasound surgery has been used successfully to produce closely defined regions of damage in the brain for neurological research, and to treat glaucoma in the eye. Its potential is now under investigation for cancer therapy. Specifically, at the Royal Marsden Hospital, we are studying the use of focused ultrasound in the treatment of liver tumours. Early results in implanted tumours in rats are promising. A potential strength of this type of treatment is that the volumes of tissue damage may be clearly seen on a diagnostic ultrasound image. Thus, the technique offers a way of producing localized tissue damage at depth within the body, while monitoring the amount of tissue damage in real time.

Ultrasound image enhancement for lithotripsy

N. P. Cohen, H. N. Whitfield, W. G. Bowsher,
J. W. A. Ramsay and R. W Miller
Lithotripter Unit, Department of Urology, St Bartholomew's Hospital, London, UK

Most second-generation lithotripters incorporate ultrasound (US) as the imaging option for the majority of urinary and biliary tract stones. Difficulties occur in defining the edge of the stone and in assessing the degree of fragmentation during extracorporeal shockwave lithotripsy. Accurate targeting is impeded by respiratory excursions which move the stone out of the shockwave focus. The human eye can only appreciate 16 levels of grey scale, but the US image has 64 levels. To utilize fully all the available US information a technique has been devised to "enhance" the video output of our Dornier lithotripter and display this new image on a separate monochrome monitor. A variable cut-off setting allows removal of grey levels outside those of the desired image, so highlighting the stone. Variable shutters can be set to restrict the image to the "field of interest". By incorporating a memory, the incoming signal from the lithotripter can be "matched" to a previously memorized stone image. The percentage match can be varied and, with a switch, allows release of shockwaves only when the stone is in the shockwave focus. With improved targeting, potential renal and perirenal damage is reduced and the number of applied shockwaves kept to a minimum to fragment the stone. One hundred and fifty-eight patients with renal stones were treated in our first 5 months using the standard US image. Renal stones are now being treated with the modified "enhanced" image and results, including applied shockwave numbers and successful clearance, will be discussed.

Initial experiences in the treatment of gallstones by extra-corporeal shock wave lithotripsy

E. B. Rolfe, J. Fielding and J. Watt
Departments of Radiology, Surgery and Anaesthetics, Queen Elizabeth Hospital, Birmingham B15 2TH, UK

Extra-corporeal shock wave lithotripsy (ESWL) provides a non-invasive method of stone disintegration. To assess the possible usefulness of this technique, a group of 17 patients (five male and 12 female) has been treated by ESWL. Age ranges have varied between 33 and 72 years. A non-functioning gallbladder or a history of previous pancreatitis are taken as contra indications to ESWL. It has been stated that calcified gallstones are also a contra indication. This did not apply to the present study. Patients received intravenous sedation and analgesics prior to treatment and a total of 2000 shocks were administered, the calculi being localized by ultrasound. Response was assessed by plain films and ultrasound examination. A total of six patients received two treatments over varying time intervals of between 4 days and 8 months. Fragmentation was achieved in the majority of patients. Of the three calcified calculi treated, breakup into multiple fragments was achieved in two. The third opaque calculus showed no response on plain film obtained immediately after treatment. Extra-corporeal shock wave lithotripsy may be useful, particularly if patients wish to avoid invasive treatment. Some opaque calculi can be fragmented. Long-term results and frequency with which stone reformation occurs will require further evaluation.

The future of lasers in cancer therapy

S. G. Bown
National Medical Laser Centre, University College and Middlesex School of Medicine, London, UK

Laser light can produce localized tissue necrosis. The carbon dioxide laser can cut and vaporize tissue with precision, but the Nd:YAG laser gives a wider range of effects of value in cancer therapy. The beam can be transmitted via flexible fibres and penetrates almost 1 cm into tissue. If surface layers are vaporized, the underlying region is coagulated, ensuring haemostasis. This makes it suitable for endoscopic palliation of advanced obstructing cancers of the gastrointestinal tract and major airways. The benefit is almost immediate and morbidity is minimal. There is no cumulative toxicity, but regular treatments are often required to maintain palliation. For oesophageal tumours, pilot studies show that laser recanalization followed by palliative external beam radiotherapy gives better and longer lasting palliation than either technique on its own. This sort of combination therapy may prove appropriate for a range of advanced cancers. This laser can also be used endoscopically to coagulate smaller tumours in patients not suitable for surgery. Routine Nd:YAG laser techniques use high power (typically 30–80 W) with the laser fibre held a few millimetres off the target tissue. A new approach is to use much lower power (1–2 W) and insert one or more laser fibres (0.2–0.4 mm diameter) percutaneously through needles into tumours in the centre of solid organs such as the liver and pancreas. The tumour and fibre positions and the development of thermal necrosis can be monitored in real time with ultrasound during 5–10 minute exposure. With sufficient surrounding normal tissue, necrosed areas heal without the need for any further intervention. Other techniques exist for producing local hyperthermia, but this technique has the advantage of precision and ease of application. It has now been applied to 10 patients with isolated hepatic metastases and three with primary pancreatic carcinomas. Local tumour necrosis without complications was seen in all, although regrowth has occurred in some. The third way in which lasers are used for cancer therapy is known as photodynamic therapy (PDT), a non-thermal technique in which systemically administered photosensitizing drugs are activated in tissue by low power laser light. These drugs are retained with some selectivity in malignant tumours, but the main advantage of PDT is the nature of the tissue damage produced. In contrast to thermal damage, full thickness necrosis of thin walled organs (*e.g.* bronchus, bowel) heals with regeneration without risk of perforation. Only small volumes of tumour can be treated, but the technique is likely to be of value for multiple small tumours (*e.g.* Ca *in situ* in the bladder) or to eradicate possible local microinvasive disease left after surgical resection (*e.g.* for rectal cancer). Laser therapy is in its infancy, but it is developing an increasing role in cancer treatment which is complementary to established modalities. However, the key to future applications lies in imaging tumours so the extent of laser damage can be matched to the extent of the lesion being treated as without this, there is no prospect of these laser techniques being curative.

Minimally invasive gall bladder surgery

J.E.A. Wickham
Academic Unit, Institute of Urology and Minimally Invasive Therapy Unit, The London Clinic, London, UK

There is now a wide menu of options for the treatment of stones in the gall bladder:
(1) open cholecystectomy,
(2) endoscopic cholecystectomy
(3) percutaneous cholecystolithotomy and
(4) extra corporeal lithotripsy. These various options are described and discussed. The decisions as to the most appropriate therapy appear to devolve upon two questions: (1) is the gallbladder healthy and functioning? and (2) what is the contained stone burden? The resolution of these questions is described from practical experience of these various techniques.

2.30 – 3.45

Radiation Protection

Norfolk Room

New radiation protection standards and their application

R. H. Clarke
Director, National Radiological Protection Board, Chilton, UK

In spring 1991, the International Commission on Radiological Protection published new recommendations, which replaced those that have existed since 1977. This paper will identify the main reasons for the changes in recommendations and will then outline the new conceptual framework for protection. Special attention will be drawn to the new dose limits for occupational exposure, including the treatment of pregnant women, and those for members of the public. Those features of the recommendations which will be of particular interest to those concerned with medical applications are highlighted.

Normalized scattered radiation data for diagnostic radiology equipment

N. W. Marshall and K. Faulkner
Regional Medical Physics Department, Newcastle General Hospital, Newcastle upon Tyne NE4 6BE, UK

Measurements of scattered radiation were undertaken on a diagnostic X-ray set over a range of tube potentials and field sizes, for both overcouch and undercouch tube geometries. A Rando phantom was used as the source of X-ray scatter, whilst the use of a PTW Diamentor dose–area product meter enabled the scatter data thus generated to be normalized for tube output variation and for the various field sizes employed during the study. The data generated were used to calculate isokerma curves for the scattered radiation for both overcouch and undercouch tube geometries. These curves are presented, along with plots of scattered radiation against field size and tube potential for various positions around the patient couch. It may be deduced from these results that, for a given position and Diamentor reading, the scattered radiation at that point can be predicted from the results at one tube potential with an accuracy of approximately 30%. It is considered that these results will have important implications in staff dosimetry. In particular, these results and this method of measurement should yield better predictions of staff doses in diagnostic radiology.

Is some of our dosimetry wrong?

P. Dawson and R. Jaeger
Department of Radiology, Hammersmith Hospital, Ducane Road, London W12 0HS, UK

Radiation dosimetry is an inexact science. The data available for doses in various radiological procedures to such organs as the ovary, bone marrow, etc. are calculated estimates and have been found, in any case, to vary enormously from department to department and from operator to operator. One factor which has not been taken into account in the calculations is the presence, during some procedures, of substantial amounts of radiological contrast agent in the tissues. This is an interesting oversight since the very purpose of radiological contrast agents is to increase the radiation absorption in the tissues. Some approximate calculations are presented which indicate that we may be underestimating the dose for some tissues and organs by a factor of two or three. The clinical implications will be discussed.

Coronary angiography: an analysis of UK patients

L. P. Readman and *R. Coulden
*Main X-ray Department, Withington Hospital, West Didsbury, Manchester M20 8LR and *Department of Cardiology, Manchester Royal Infirmary, Manchester M13 9WI, UK*

Cardiac catheterization is the "gold standard" for imaging the left ventricle and coronary arteries (LV and cors). Despite its widespread use, there is no consensus as to how it should be performed. Different operators use different radiographic projections, numbers of projections and cine frame rates. This may result in wide variations in the ionizing radiation that a patient receives. As part of the development of a standard examination protocol for LV and cors, we set out to establish the range of practice in the UK. A questionnaire was sent to all invasive cardiac units asking for the following information. For a routine LV and cors, (i) what are the standard projections, image intensifier format and cine frame rate and (ii) what is the average patient dose and screening time. Replies were received from 35 of 48 centres (73%). The number of projections used ranged from 7 to 12 (LV 1–2, right coronary 2–4, left coronary 4–7). Frame rates varied from 12.5 to 50 fps and both small and large image intensifier formats were used. Average screening time was 4.3 mins (range 1.5–15 mins). Only five centres (14%) gave a radiation measurement for the entire examination, five others gave a measurement per digital/cine frame. The remaining 72% were unable to answer. The survey shows great variations in technique throughout the UK. These all have important radiation dose consequences and are hard to justify. A consensus examination protocol, derived from the survey, is proposed.

^{131}I labelled mIBG therapy for neuroblastoma in young children: radiation doses received by parents and other relatives

S. Packer and C. Taylor
Medical Physics Unit, Cookridge Hospital, Leeds LS16 6QB, UK

The treatment of neuroblastoma using ^{131}I mIBG requires the administration of large amounts of radioactivity as an unsealed source. Many of the children treated are very young and therefore incontinent and unable to care for themselves. They are also too young to "entertain" themselves when placed in the semi-isolated treatment rooms required for unsealed source therapy. These children require a lot of contact with their parents and other family members who therefore receive significant radiation doses. Measurements of doses received by parents of children undergoing such therapy have been made. The results show that a large proportion of their radiation doses are received prior to therapy, while the patient is undergoing diagnostic studies and after discharge when the amount of activity in the patients is very low when compared with the amount administered for the therapy. Total radiation doses to parents are such that it is possible that limits for members of the public will be exceeded. Proposed reductions in dose limits will make this a near certainty.

Doses to radiologists doing cardiac catheterization procedures

C. Taylor and S. Packer
Department of Medical Physics, Cookridge Hospital, Leeds LS16 6QB, UK

Radiation doses to staff undertaking cardiac catheterization procedures are among the highest of any radiological examination, since they involve lengthy fluoroscopy screening times and require close proximity to the main X-ray beam. Body dosemeter readings often underestimate doses received because the dosemeter is shielded by the protective apron. In this study, measurements of doserates encountered by those performing procedures have been measured. In addition, doses to unprotected parts of the body have been estimated by means of thermoluminescent dosemeters worn on the hands and neck. Dosemeter results have been combined with records of fluoroscopic screening times to give doses related to workloads. The workload related doses are compared with the results of doserate measurements, and with the results of routinely worn body dosemeters.

Radiation doses to paediatric patients undergoing special radiographic procedures

C. L. Chapple, K. Faulkner, *R. Lee and *E. Hunter
*Regional Medical Physics Department, Newcastle General Hospital, Newcastle upon Tyne NE4 6BE, and *Radiology Department, Royal Victoria Infirmary, Newcastle upon Tyne, UK*

A semi-automated dosimetry survey has been undertaken to monitor the radiation doses to patients in a paediatric special procedures X-ray room. Patient doses were assessed both by using thermoluminescent dosimeters attached to the patient's skin at various anatomical positions, and by using Diamentor ionization chambers to measure dose–area products. The radiographer enters information on the patient and examination technique into a computer, which then automatically reads and resets the Diamentor. All information is stored on a computer database. A large number of fluoroscopic examinations have been monitored, including renal and jejunal biopsies, nephrostograms, loopograms, tracheograms, fistulograms and duodenal intubations. The results of the survey will be presented. The radiation doses from these interventional radiological procedures will be compared with those from other paediatric examinations.

Radiation dose to patient and personnel in extracorporeal shock wave lithotripsy

C. Baldock and T. Greener
Medical Physics Department, St Thomas' Hospital, London SE1 7EH, UK

Extracorporeal shock wave lithotripsy (ESWL) has become the primary choice of treatment for patients with renal and upper ureteral calculi. This form of treatment uses either X-ray fluoroscopy and/or ultrasound to localize the calculi and to determine the end point of treatment. Work has been reported in the literature on radiation doses received from the Dornier and Siemens Lithostar ESWL systems. We report radiation doses measured to patients and personnel from the Storz Modulith lithotripter system installed in the Lithotripter Centre, St Thomas' Hospital, London.

Norfolk Room

Radiation dose to the eye and thyroid gland in high resolution computed tomography of the pituitary gland

L. P. Readman, *K. Faulkner and §J. E. Adams
*Main X-ray Department, Withington Hospital, West Didsbury, Mancheter M20 8LR, §Department of Diagnostic Radiology, University of Manchester, Manchester M13 9PT and *Department of Physics, Christie Hospital, Manchester M20 9BX, UK*

Patients undergoing neuroradiological investigations may receive a significant radiation dose to the eye. High resolution computed tomography (HRCT) is an accepted method for the detection and assessment of pituitary adenomas. Imaging in the direct coronal plane is preferred to the transaxial plane because the radiation dose to the eye is lower. However, not all patients can achieve or maintain the position of the head required for direct coronal scanning. In this situation, imaging is performed in the transverse axial plane and from these data coronal and sagittal reformations can be obtained. The study was undertaken to measure the radiation dose to the eye during such an examination. The radiation doses to the eye and the thyroid gland were measured during a simulated HRCT examination of the pituitary. Fifteen contiguous 1.5 mm sections were performed through the pituitary fossa in two planes. The first plane was parallel to the orbitomeatal baseline (OMBL) and passed through the superior orbital margin; the second was at an angle of -10 to the OMBL. This passed directly through the eye. The measurements were made using lithium fluoride thermoluminescent dosemeter rods in purpose-built holders over the eye. The thyroid doses were measured using thermoluminescent dosemeter sachets. It was confirmed that a radiation dose reduction of 89% to the lens of the eye could be achieved by selection of the appropriate transaxial scanning plane.

* Present address: Regional Physics Department, Newcastle General Hospital, Newcastle Upon Tyne.

Use of a database to analyse patient doses from radiographic examinations and assist in their reduction

C. J. Martin, C. Darragh, G. McKenzie and J. Weir
Departments of Bio-Medical Physics and Bio-Engineering, and Radiology, Aberdeen Royal Infirmary, Grampian Health Board, Foresterhill, Aberdeen AB9 2ZD, UK

The paper describes the strategy being adopted by Grampian Health Board, with physicists, radiographers and radiologists working together to reduce patient doses. A database on an IBM PC is being used to store data from QA tests on all X-ray equipment operated by the Grampian Health Board. Exposure factors are combined with output measurements to calculate patient entrance skin doses for standard examinations. Data are displayed in the form of bar charts, which can readily be interpreted by other staff, comparing the entrance dose for each projection with a reference level put forward by the National Radiological Protection Board. Units giving higher entrance skin doses are identified, and thermoluminescent dosemeter measurements carried out to confirm the results where necessary. Radiographers, physicists and radiologists consult to determine factors responsible for high doses, and identify appropriate corrective action. Practical experience in the implementation of this strategy for dose reduction will be discussed. Where results for all examinations have been high, the effects of processing conditions, *e.g.* developer temperature and replenishment rates, speeds of film/screen systems, grid ratios and absorption rates of X-ray table tops and vertical stands, were considered as possible contributory factors. High results for particular examinations have been due to differences in radiographic technique.

Evaluation of a Diamentor

G. D. Morrison, M. T. Davies and B. Garner
Department of Clinical Physics and Bioengineering, Guy's Hospital, Cunliffe Laboratories, London SE1 9RT, UK

Tests were carried out on the performance of the Diamentor dose–area product exposure meter in diagnostic radiology. The Diamentor was tested against the manufacturer's specifications and the evaluation of Shrimpton and Wall (1982). These tests included the energy and dose rate response of the chamber, its aluminium equivalent filtration and the accuracy of its calibration. Following on from the technical assessment, the clinical usefulness of the device was evaluated. A survey of the exposures from a lumbar spine examination was carried out in the Radiology Department of Guy's Hospital. Readings were taken from several hundred patients. For 20 patients, thermoluminescent dosemeters were also used to measure the entrance skin dose for each film. From these results the effective dose equivalent for the examination was calculated using National Radiological Protection Board (NRPB) organ dose factors and International Commission on Radiological Protection organ weighting factors. The Diamentor was found to comply favourably with its specification. A variation of ±5% with energy was found against an MDH 1015 electrometer in the range 60 – 120 kVp. It was possible to calibrate the unit to ±5%, with a consistency between exposures of ±0.6%. Clinically, the Diamentor was easy to use and permitted a comparison between national exposure values, as published by the NRPB, and those measured locally.

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Monday 29 April

Diagnostic Radiology (4.15–6.00)

Lancaster Room

Teaching of postgraduate students in the 1930s

J. A. Ross
Eagle Crag, 3 The Nook, Frankby Green, Merseyside, L48 1PH

This is a short account of teaching of postgraduate students of radiology in the 1930s. The writer was fortunate in joining the staff as a registrar in the X-Ray department of the Manchester Royal Infirmary. Twining's early efforts to produce a simplified form of tomograph which became universal are described. His early work on cerebral arteriography is referred to, which greatly assisted Sir Geoffrey Jefferson. Reference is made to his magnificent writing describing the radiology of diseases of the chest in the edition of the volume produced by British Authors for Messrs. H. K. Lewis.

Early experience with percutaneous cardiopulmonary support in percutaneous transluminal coronary angioplasties and resuscitation

U. M. Sivananthan, M. R. Rees, T. Browne, S. Whittaker and
G. A. Davies
Department of Radiology, Killingbeck Hospital, Leeds, LS14 6UQ

The recent introduction of portable self-contained cardiopulmonary bypass systems together with vascular access via percutaneous cannulae has extended the role of extracorporeal circulatory support into coronary angioplasty and resuscitation.
The vascular access is via femoral vessels using a modified Seldinger technique with siting of the 17 F to 19 F cannulae at the junction of the vena cavae and right atrium, and common iliac artery. The closed circuit system consists of a constrained Vortex pump, oxygenator and heat exchanger. Outputs of up to 6l/min may be obtained. A total of 19 patients (IBM: 3F) underwent percutaneous cardiopulmonary support (CPS); eleven of the patients were judged to be high risk (low ejection fraction, target vessels supply greater than 50% of the viable myocardium, surgically inoperable etc.) for percutaneous transluminal coronary angioplasties (PTCA) and were electively supported by CPS. Eight patients underwent emergency CPS as part of resuscitation and four of these patients survived to undergo PTCA. One patient was supported during aortic valvuloplasty. Five deaths occurred in total, significantly all in the emergency CPS group. We have found CPS a useful adjunct in elective PTCA for high risk patients. All 10 of the 11 elective CPS patients who would ordinarily not have been considered for angioplasty underwent successful PTCA. But this relatively new procedure needs further evaluation before being widely used.

Magnetic resonance imaging of normal and internally deranged temporo-mandibular joints

A. Brady, *L. McDevitt and J. Stack
*Institute of Radiological Sciences, Mater Misericordiae Hospital, Dublin 7, Ireland and *School of Dentistry, Dublin University, Dublin 2, Ireland*

Magnetic resonance imaging of 72 temporo-mandibular joints in 36 subjects was performed on a 1.5 T unit. T_1-weighted parasaggital images were obtained in closed-mouth, intermediate and maximum-passive-opening positions. Coronal T_1-weighted images were obtained in the closed-mouth position. Clinical assessment of the joints was performed independently of MRI, based on history, clinical examination, joint axiography and sound recordings during joint movement. The images were reported by two radiologists, blinded to the clinical status of the patient. 31 (91.2%) of 34 clinically normal joints were reported as normal on MRI. One clinically normal joint was reported as showing a reducing disc displacement. 20 joints clinically had reducing disc displacements. 15 (75%) of these were reported as such on MRI. Three were reported as normal and two as showing non-reducing disc displacement. 18 joints had clinically non-reducing disc displacements. 10 (55.5%) were reported as such on MRI, three reported as normal and three were as reducing displacements. In four joints, disc position was not ascertained on MRI. Overall, correlation between clinical assessment and MRI interpretation occured in 77.7% of joints. We believe that MRI offers a reliable, non-invasive assessment of morphology in the normal and internally deranged TMJ superior to any other non-invasive radiologic technique.

Three-dimensional imaging of right ventricular function using gated blood pool tomography

S. Cross, H. S. Lee, M. Norton and S. Walton
Departments of Cardiology and Medical Physics, Aberdeen Royal Infirmary, Aberdeen, AB9 2ZB, Scotland.

Tomographic imaging of the cardiac blood pool has been shown to be useful for studying the left ventricle. Regional right ventricular function is difficult to examine non-invasively: the right ventricle does not contract uniformly and differs in shape and size between individuals. We describe our findings in examining the right ventricular phase maps in a group of patients undergoing gated blood pool tomography. After labelling of the red blood cells with technetium, tomographic sections of the cardiac blood pool were obtained in 55 patients admitted for cardiac catheterization. The images were displayed as a pseudo three-dimensional image on a computer screen. The phase images of the right ventricular blood pool in 20 controls were compared to those obtained in 35 patients with previous myocardial infarction (MI). There were focal areas of abnormal right ventricular phase in 10/15 patients with inferior MI, and in 1/20 patients with anterior MI. Our results show that three-dimensional gated blood pool tomography can be used for the study of abnormal right ventricular contraction.

Improving throughput in magnetic resonance imaging; the Oxford approach

N. M. Moore and S. J. Golding
Department of Radiology, University of Oxford, Oxford, OX2 6HE

A major factor governing patient throughput in magnetic resonance imaging (MRI) is the number and duration of the sequences used. The Oxford MRI Group has investigated the practical implications of applying on a selective basis strict standardized protocols to the examinations of the brain, lumbar spine and knee.

170 patients were allocated to the study on putative suitability for this approach. Examinations were assessed by comparison with target duration, and by efficacy as defined by confidence levels in reporting and by rate of recall, if necessary. Successful examinations of 20 min duration were carried out for the brain ($n=113$), knee ($n=23$) and lumbar spine for disc degeneration ($n=13$) in 97%, 87% and 69% of patients respectively. Examinations of the spine for radicular symptoms ($n=21$) were completed in 30 min in 86% of patients. We describe the indications we accepted, the individual time components, and methods by which these results could be improved further. Selected patients can undergo successful MRI studies in short examination times. Instituting this approach generally could increase patient throughput by 80–125%. This study has significant implications to the length of waiting lists and availability of MRI in the UK.

Painful knee arthroplasties: does digital subtraction arthrography help?

J. Namasivayam, A. Forrester and F. W. Poon
Department of Diagnostic Radiology, Royal Infirmary, Glasgow, G31 2ER.

20 Patients with painful knee arthroplasties were studied prospectively with digital subtraction arthrography. 10 patients had the arthrogram carried out in a lateral projection (Group 1) and 10 in an antero-posterior projection (Group 2). In Group 1, five patients had loosening of both tibial and femoral components and two patients had loosening of the tibial component. In Group 2, three patients and loosening of the tibial component. All 10 patients with loosening had revision arthroplasty and the radiological findings were confirmed except for one tibial component loosening which was undetected in the lateral projection. We conclude that digital subtraction arthrography is a useful method of assessing the problem arthroplasty. Our results suggest that arthrogram of the knee in the lateral projection may provide more information that the antero-posterior projection. However, arthrographic projections should be tailored more closely to the clinical findings.

A new application for effervescent agents in the small bowel meal examination

P. D. Griffiths and D. F. Martin
Department of Radiology, Withington Hospital, Nell Lane, Withington, Manchester

We present data concerning a new application for the use of effervescent granules during full small bowel meal examination that is intended to speed up the examination. 24 patients referred to the department for small bowel examinations were randomly placed into two groups. The control group received the standard small bowel meal technique as practised in this department. This involves prior bowel preparation, and the patients are given 15 mg metaclopramide hydrochloride (maxolon) orally. 15 min later the patients start to drink 450 ml of 30% baruim suspension (E-Z paque). The study or "carbex" group receive indentical preparation; however, the barium administered also contains 16.8 g of effervescent granules (six sachets of carbex). Note that the carbex fluid is not given. The time the barium took to reach the caecum, the screening time and the room time were recorded. A consultant radiologist assessed the qualtiy of each examination (DFM). The results indicate that the use of effervescent granules in the barium used for SBM significantly reduces the time taken to reach the caecum. Patient acceptibility and diagnostic quality were not significantly altered.

	Transit time (min)	Screening time (min)
Control	56 ± 36	4.4 ± 1.9
Carbex	12 ± 4	2.0 ± 0.7
Student's t test	$p < 0.01$	$p < 0.05$

The influence of bowel preparation on segmental transit in patients with idiopathic slow transit constipation using oral ^{111}I-DTPA scintigraphy

J. Roberts, D. Waldron, M Newell, N. Garvie and N. Williams

Surgical Unit and Radioisotope Department, The Royal London Hospital, Whitechapel Road, London, E1 1BB

In idiopathic slow transit constipation (STC) delayed transit occurs in the transverse colon and splenic flexure. This could be due to a primary abnormality of motility in these areas or to distal obstruction. To investigate these possibilities six patients with STC, being considered for colectomy, underwent scintigraphy in unprepared bowel and after bowel clearance with sodium picosulphate and rectal washout. 3.8 MBq of ^{111}I-DTPA was taken orally in water. Anterior andposterior scans were taken at 18 h and at intervals until 96 h. Six regions of interest (ROIs) were drawn around the colonic images. Percentage activity curves for each ROI and the centre of gravity of the isotope (COG) were calculated after attenuation and decay corrections had been made. Delayed right sided emptying was seen in all scans. Washout did significantly change either the percentage activity or the COG curves. Activity accumulated in the transverse colon and splenic flexure reaching 80% (27–88%)* in unprepared and 69% (32–72%)* in prepared bowel at 96 h. COG at this time was 3.58 (3–5.8)* and 3.7 (3.5–4.6)* respectively. Accumulation of isotope in the transverse colon and splenic flexure of patients with STC appears to be a localized abnormality and not secondary to distal obstruction.

*Median and (range).

Side effects of Picolax^R in patients having barium enemas

J. A. L. Lawrance, T. F. Massoud, D. J. Nolan, W. Shatwell, A. Mason and T. Creasy

Department of Radiology, John Radcliffe Hospital, Oxford, OX3 7HN

This is a prospective, single-blind trial to determine the effect of various fluid regimens on the side effects of sodium picosulphate. Patients received two sachets of Picolax^R and were randomized into one of five fluid regimes on the day prior to the enema. (Group 1: 4 pints of Dioralyte^R (electrolyte and glucose solution). Group 2: 4 pints of Water. Group 3: 6 pints of water. Group 4: 4 pints of half-stength Dioralyte^R. Group 5: Free fluids.) Symptoms were gradedsamples obtained prior to the enema. The first 100 patients have been analysed to date. Those on 4 pints of Dioralyte^R had the least mean headache score. Mean headache score: Group 1 = 1.24 (standard error (SE) 0.31), Group 2 = 2.29 (SE 0.48), Group 3 = 1.69 (SE 0.41), Group 4 = 2.15 (SE 0.37), Group 5 = 2.00 (SE 0.41). Electrolyte and glucose supplementation may thus be useful in reducing headache in patients having Picolax^R. Interestingly, there has been no correlation between mean plasma osmolality and the headache score. Other authors have suggested an association between dehydration and headaches after Picolax^R, while this study shows no difference in osmolality between those patients who do not develop headaches and those who do.

^{99}Tc^m methoxy isobutyl isonitrile in the assessment of peripheral vascular disease

K. A. Miles, *M. Cooper, *D. S. Appleton, +R. W. Barber and E. P. Wraight

*Departments of Nuclear Medicine, *Radiology and +Medical Physics, Addenbrooke's Hospital, Cambridge, between 0 and 5 (none too severe) and blood and urine ACB2 2QQ*

Assessment of leg blood flow in peripheral vascular disease (PVD) with radionuclides provides functional information which is complimentary to the anatomical information from angiography and has previously been performed using ^{201}Th or ^{99}Tc^{m} labelled red blood cells. We describe a new technique for measuring calf and thigh blood flow as a proportion of cardiac output (BF/CO) using ^{99}Tc^{m} methoxy isobutyl isonitrile (^{99}Tc^{m}- MIBI). Eight patients with PVD undergoing contrast angiography and four with no history of leg claudication were examined at peak treadmill exercise and at rest. Normal resting and exercise calf BF/CO were 0.73% and 1.77% respectively. In PVD resting calf flow was slightly reduced at 0.57% ($p < 0.05$) but exercise flow was markedly lower than controls at 1.01% ($p<0.00001$). Exercise calf BF/CO correlated with the angiographic severity of PVD. Exercise thigh BF/CO was also reduced in PVD ($p<0.005$) but there was no correlation with angiographic severity. Emission tomography demonstrated regional ischaemia within specific muscle groups of the calf in somepatients. An increase in calf blood flow was demonstrated following angioplasty. ^{99}Tc^{m}- MIBI is potentially useful in the assessment of PVD and it has advantages over other methods of assessment.

A study of skin entrance doses for low kVp chest radiography

A. J. Hunt and J. Fisher
Department of Medical Physics, Poole General Hospital, Longfleet Road, Poole, Dorset, BH15 2JB

Following recent national reports of a wide variation in patient radiation doses from a range of common radiographic examinations, it was decided to investigate the variation in patient skin entrance doses for PA chest studies throughout our X-ray Department. The measurement technique chosen was Lif TLD pellets, placed on the skin surface of 50 patients for each of seven rooms.

The variation in patient thickness and sex, age along with kVp and mAs were noted. Other considerations were screenspeed, processing conditions and clinical acceptability of the radiograph. Comparison both between rooms and with the national picture, along with investigation of the reasons for any variations, is underway. The results thus far suggest that there is significant variation in the skin entrance dose between rooms. Variation within individual rooms appears to be less marked. The mean dose for this hospital compares favourably with the national picture.

A real expert system for assisted instru[illegible] radiologist students

D. Neamtu, G. Saplacan, A. Radulescu, M. Bocu, S. Selinger, M. Vaida and S. Sfrangeu
C51, Institute for Computer Technology, Cluj-Napoca 3400, Romania

Our system was created to integrate the patie[illegible] available medical information and allow its use for assisted instruction of the students. The entire system needs an IBM personal computer with an image interface, a VGA and a hard disk. A database was implemented for the Department of Angiography. The medical database contains: general information about patient and examination results using the examination methods Doppler oscilometry, thermography and angiography. The images taken by the angiograph are digitized by the image interface, and stored on the PC's hard disk. Here local image processing is possible. Images are transferred on magnetic support. The medical data from the database and information concerning the medical images are used by the expert system for diagnosis and assisted instruction. The user interprets the medical images displayed on the PC's screen. The students may acquire knowledge of diagnosis for different illnesses at the level of medical experts. After the domain expert knowledge of the system is loaded, it can be used by an unspecified number of students who can work on real cases. The system can check the degree of expert knowledge achievement, by using the instruction part to find out the rules the students do not know or cannot use properly, and also the students' abilities to discover useful information from medical images. By modifying the expert knowledge of the system, it can be used without further changes for any other medical domain in which medical images are used for diagnosis.

Assessment of bladder volume by ultrasound: a comparison of different methods

V. C. Williamson, H. Kynaston, G. Lamb and K. F. Parsons
Department of Radiodiagnosis, Royal Liverpool Hospital, Prescot Street, Liverpool, L7 8XP

Two methods of assessing bladder residuals have been evaluated in 100 patients undergoing urological assessment for outflow obstruction/instability: (1) direct ultrasound measurement; (2) subtraction of the voided volume from an ultrasound measurement of full bladder volume. Realtime ultrasound bladder scans were performed on 100 patients.

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A comparison of two techniques of radiography for aortography

Y. Washington and M. J. Raphael
Department of Radiology, The Middlesex Hospital, London, W1N 8AA

Two different radiographic techniques for peripheral arteriography became available with the installation of a new angiographic room. Patients were randomly allocated to conventional large film (14 x 14 in) with stepping table radiography, or 105 mm photofluorography with visual panning radiography. These two techniques were supplemented by intra-arterial digital subtraction angiograms if indicated. The total procedure time and total costs of disposables were recorded for each case. Radiation doses incurred by patients using each technique were sampled. 25 patients were costed for each technique and radiation measurements were made on 10 patients using each technique. The referring vascular surgical team was asked to evaluate the angiograms for ease of viewing and diagnostic content. The cost of disposables and the incurred radiation for large films was £114.55 and 3.19 mSv, and for photofluorograms was £102.58 and 0.59 mSv. Thus photofluorograms were on average £12.00 per examination cheaper and incurred about one fifth the radiation dose of larger films. The vascular surgeons regarded them as of adequate diagnostic quality, with the additional advantage of ease of viewing since the photofluorograms were mounted in cardboard mounts and could easily be viewed in order. Mounted examinations could be contact copied to provide a separate departmental archive, reducing the problems of lost angiograms.

A comparison of the functional effects of diatrizoate, ioxaglate and iotrolan on the isolated perfused rat kidney

P. W. G. Brown, J. Haylor, A. M. El-Nahas and S. K. Morcos
Department of Diagnostic Imaging, Northern GeneralHospital, Sheffield, South Yorkshire, S5 7AU

The effects of sodium-meglumine diatrizoate ($n=4$) (an ionic monomer, 300 mgI/ml osmolality 1600 mosmol/kg/ H_2O) and ioxaglate ($n=4$) (an ionic dimer, 300 mgI/ml, osmolality 550 mosmol/kg H_2O) and iotrolan ($n=4$) (a non-ionic dimer, 300 mgI/ml, osmolality 320 mosmol/kg H_2O) on renal function were studied using the isolated perfused rat kidney. The model permits evaluation of the direct renal effects of contrast media independent of their systemic influences. Kidneys were perfused at constant pressure (100 mmHg) in a recirculating system with 150 ml of perfusate based on Krebs-Heinseleit solution. After a 40 min equilibration period renal function parameters were measured over a 10 min control period. 10 ml of contrast medium was then added to the perfusate reservoir (20 mgI/ml) and furthermeasurements taken during a 30 min experimental period. All three agents caused a significant reduction ($p<0.05$) in glomerular filtration rate (diatrizoate, 40%; ioxaglate, 49%; iotrolan, 39%) and perfusate flow (diatrizote, 27.7% ioxaglate, 35%; iotrolan, 24%) compared with the control period. The functional parameters of kidneys perfused without the addition of contrast remained stable throughout the control and experimental periods. In conclusion, diatrizoate, ioxaglate and iotrolan cause a similar significant impairment of renal function through a direct mechanism. The effects appear to be independent of osmolality and are likely to be influenced by the chemical composition of the contrast agents.

Work in Progress: L

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The limiting values of the relevant parameters were described and submitted for possible agreement with a view to proposing their standardisation.

Radiologists, radiographers, medical physicists, manufacturers of X-ray equipment and regulatory bodies, whether developing new quality assurance programmes, or reviewing existing ones, or deciding about technological improvements or health care and radiation protection investments will find this book a useful reference.

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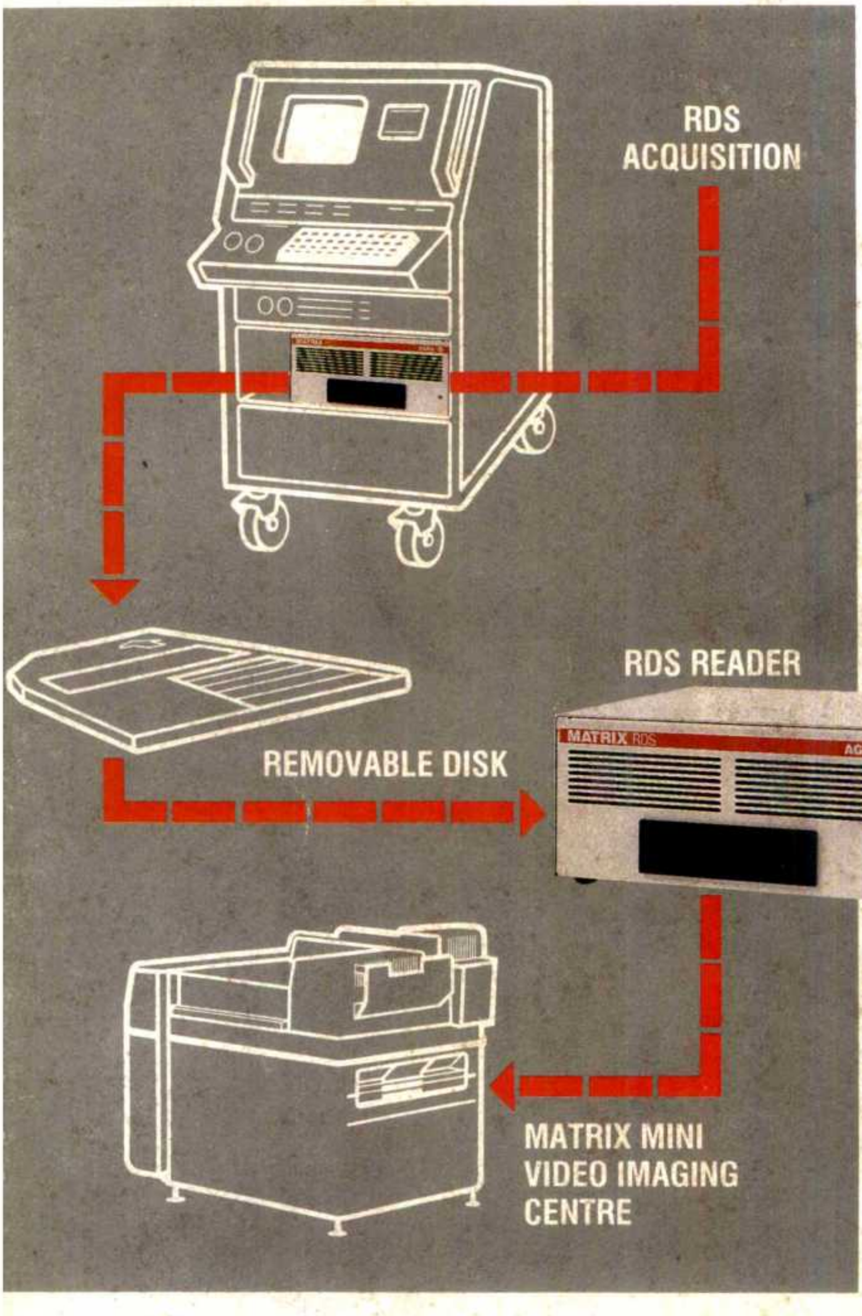

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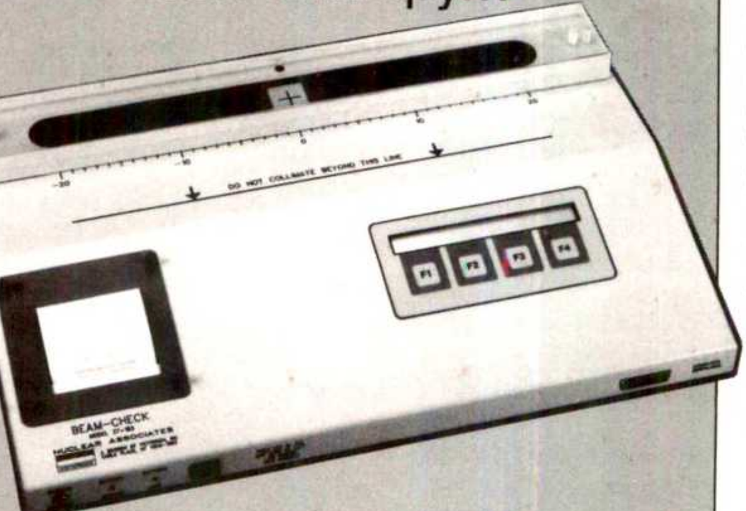

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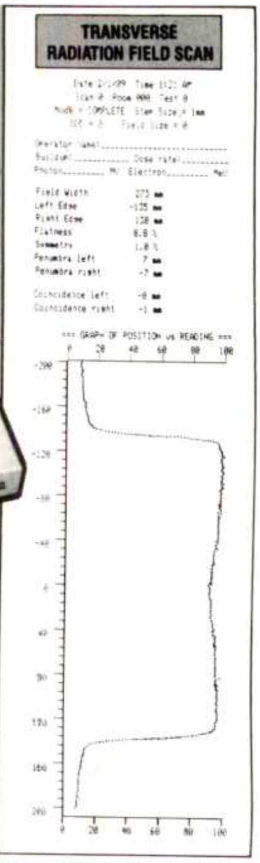

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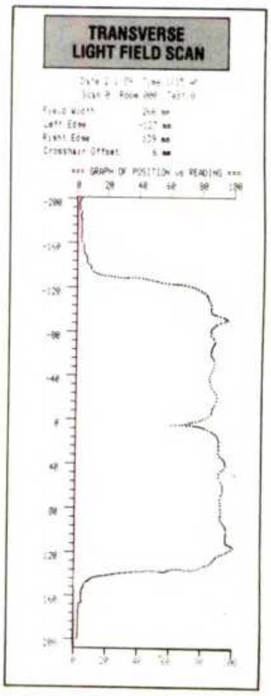

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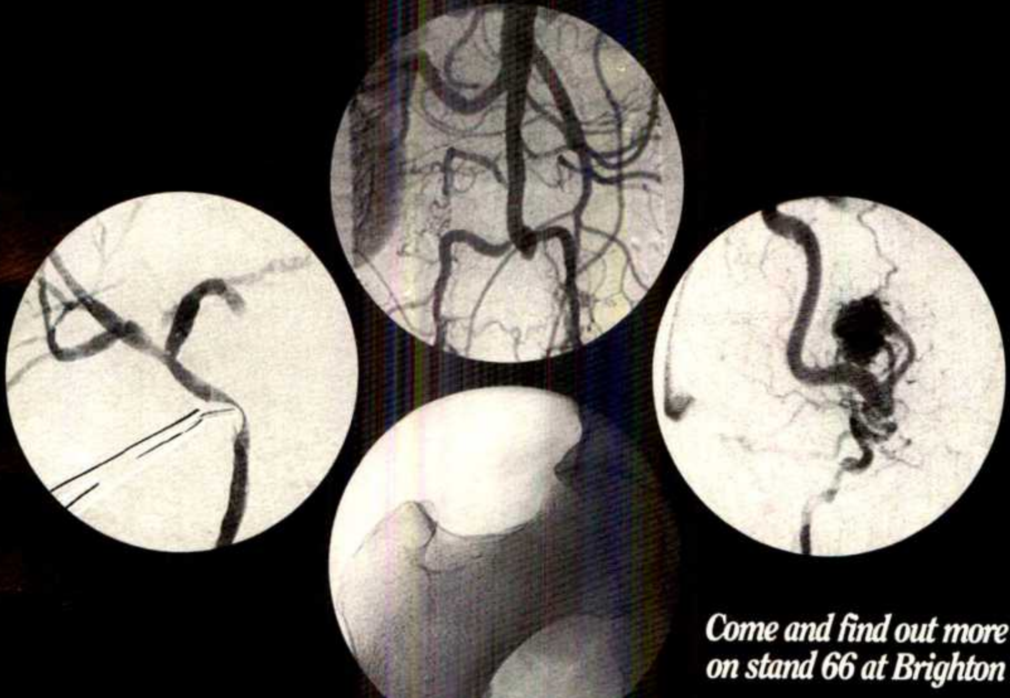

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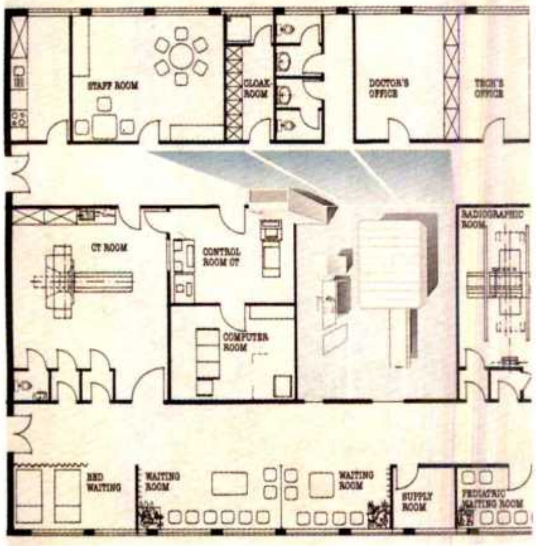

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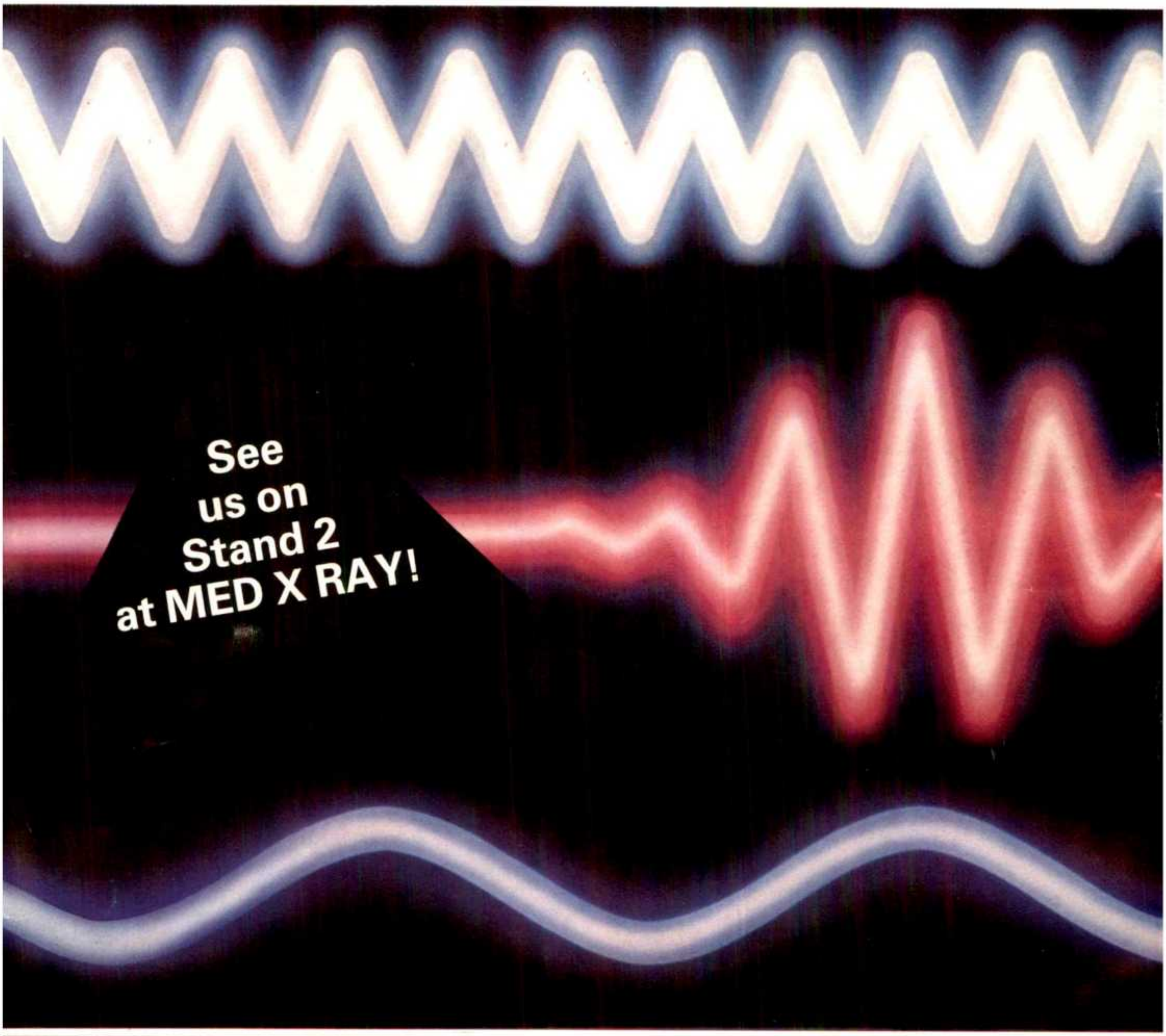

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Monday 29 April

Diagnostic Radiology in Tumours, Biopsy Techniques (10.45–12.00)

Lancaster Room

Repeated ablation of giant bone metastases with absolute ethanol

K. Choji, Y. Ubayama, M. Ogasawara, Y. Sato, K. Kubo and G. Irie
Department of Radiology, Hokkaido University Hospital, Sapporo 060, Japan

Transcatheter injection of absolute ethanol is an effective method of producing tissue ablation and vascular occlusion. Indications for this procedure include palliative tumour infarction for pain relief, pre-operative reduction of blood flow and tumour bulk. Repeated ablation of large bony metastases has not been previously documented. We therefore report our initial experience in two patients with bony metastases from hypernephroma. The first case presented with a large metastasis in the ileum amenable to hemipelvectomy. Pre-operative repeated ablation of the metastasis with absolute ethanol resulted in destruction of the feeding vessels and disappearance of the tumour on arteriography and bone scintigraphy, thus avoiding the need for surgery. In the second case the patient had a large solitary bone metastasis in the ileum. Owing to intractable pain, repeated ethanol ablation was undertaken, resulting in near-total destruction of the feeding vessels and development of a photopenic defect on bone scintigraphy. Our initial experience indicates that repeated ablation of large bony metastases is a promising means of local tumour control. Repeated ablation allows selective delivery of small volumes of ethanol and minimizes non-target complications.

Bronchiolo-alveolar carcinoma: a review of the radiological appearance in 16 cases

B. Trotman-Dickenson and F. W. Wright
Department of Radiology, Churchill Hospital, Oxford OX3 7LJ

Bronchiolo-alveolar carcinoma accounts for about 1 – 5% of primary malignant tumours. The clinical course may be long and the onset insidious. It may occur as a scar-cancer. Some consider it a variant of adenocarcinoma. We have reviewed 16 patients (seven women and nine men) with bronchilolo-alveolar carcinoma. Most were elderly and smokers; cough was a frequent complaint but bronchorrhoea rare. Two survived for 8 years and three others for over 4 years. Radiological signs depend upon the amount and degree of spread by the three main routes — lymphatic, lobar (via the pores of Kohn) and bronchopneumonic. A small peripheral nodule may spread locally to give the "galaxy" or "cocklebur" signs. Lobar spread mimics pneumonic consolidation, and bronchopneumonic spread "bronchopneumonia" with disseminated areas of infiltration in both lungs. Patients may also show lymphangitis carcinomatosa and multiple miliary or larger lung nodules. Tomography (including CT) demonstrates well the infiltrative nature of the disease, the dissemination and air bronchograms, often with a characteristic "leafless tree" appearance. Cavitation was seen in two cases. Osteoblastic metastases were a terminal event in two patients owing to haematogenous spread. Only one had a pleural effusion, which was small. No brain or liver metastases were seen.

A comparison of ^{111}In and ^{125}I for intra-operative radioimmunolocalization of 28 colorectal cancer patients

J. W. Dawson, W. Waddington, B. R. Davidson, M. Short, C. Dean and P. B. Boulos
Department of Surgery and Nuclear Medicine, University College and Middlesex School of Medicine, London WC1E 6JJ

Intra-operative probing using a high energy radionuclide for external imaging may present difficulties because of background counts. We compared probing and biodistribution in two groups of patients undergoing resection for colorectal cancer, after labelling the antibody ICR2 with 100 MBq of either ^{111}In or ^{125}I. Patients were probed at laporotomy 3 days (^{111}In) or 10 days (^{125}I) after injection and the ratio of counts from tumour:normal colon (T/NC) obtained. Further probing ratios were obtained after the specimen was resected and radioactive counts from biopsies of tumour and normal tissues were measured in a gamma well-counter. Blood and urine samples were collected for 10 days. In both groups, intra-operative T/NC ratios did not differ significantly (^{125}I: T/NC 1.1 - 5.8, median 1.75. ^{111}In: T/NC 0.9 – 2.13, median 1.66) and ratios were better in the resected specimens (^{125}I: 1.0 – 7.2, median 3.1. ^{111}In: 1.23 – 6.8, median 4.7). The ratio of radioactivity per gram of tumour/normal tissues was the same in each group (^{125}I: 0.6 - 9.3, median 1.6. ^{111}In: 1.0 – 3.5, median 2.1). Plasma clearance did not differ between groups (42% injected dose present in blood at 48 h) but ^{125}I labelled patients showed 55% urinary excretion of activity in 48 h compared with only 26% in the ^{111}In group. Probing was not impaired using a high energy radionuclide such as ^{111}In. We suggest the use of a radionuclide allowing pre-operative imaging as well as intra-operative tumour identification.

Mammograms at different compression plate widths for the detection of breast cancer

R. P. Highnam, J. M. Brady and B. Shepstone
Department of Radiology and Computing Laboratory, Oxford University, John Radcliffe Hospital, Oxford, OX2 3QD

Mammographic signs are sometimes non-specific if not ambiguous. It is proposed that by taking mammograms of the same breast at slightly different compression plate widths important additional information becomes available. This information relates to the physical properties of the tissue, such as hardness and breast structure, such as when a mass is attached to the chest wall. To date, three pairs of mammograms have been obtained for study, and it is clear that extremely useful information can be derived from them by alternating the mammograms in each pair very quickly. This produces a 3D impression of the internal structures in the breast. In one case bright "calcification" is shown to disperse upon extra compression; in another a composite shadow is formed, and in the third case a spiculated mass is shown to adhere to the chest wall, whilst apparent fibrous tissue around it moves appreciably. Taking mamograms at slightly different breast compression plate widths is a potentially useful medical tool. Further work is obviously needed to ascertain how normal and abnormal structures respond, but the results so far are encouraging.

Duplex Doppler sonography in the detection of colorectal hepatic metastases: preliminary results

E. Leen, *J. Goldberg, J. Robertson, G. R. Sutherland and *C. S. McArdle
*Department of Radiology and *University Department of Surgery, Royal Infirmary, Glasgow G31 2ER*

Conventional imaging techniques are not sensitive enough to detect small liver metastases. Dynamic scintigraphy has shown that the subtle changes in liver perfusion associated with hepatic metastases may be used to detect their presence but there have been doubts about its reliability. In this study we evaluated the use of Doppler sonography (a direct method of flow measurement) to detect colorectal hepatic metastases. Hepatic arterial and portal venous blood-flows were measured in 54 patients with colorectal cancer and 16 controls. The ratio of hepatic arterial to total liver blood flow (Doppler perfusion index, DPI), the ratio of hepatic arterial to portal venous blood flow (Doppler flow ratio, DFR), and the ratio of hepatic artery to portal vein cross-sectional areas (area ratio, AR) were calculated. Clear separation of the DPI and DFR values of controls and patients with histologically confirmed liver metastases was observed (p=0.0001) and there was a significant increase in AR values in the metastases group. The data suggest duplex Doppler sonography has the potential to detect small liver metastases.

	Controls (n = 16)	Overt liver metastases (n = 33)	Disease free liver (n = 21)
L	0.13 ± 0.07	0.52 ± 0.13	0.37 ± 0.14
DFR	0.15 ± 0.09	1.27 ± 0.71	0.66 ± 0.36
AR	0.13 ± 0.05	0.36 ± 0.24	0.23 ± 0.11

^{131}I-MIBG imaging in benign and malignant phaeochromocytoma

S. Senan, N. S. Reed and *H. Gray
*Department of Radiotherapy and Oncology, Western Infirmary, Glasgow and *Department of Nuclear Medicine, Royal Infirmary, Glasgow G11 6NT*

^{131}I labelled MIBG has an established role in the imaging of phaeochromocytomas with up to 90% of tumours reported to show uptake. We describe our experience with 19 patients having histologically proven phaeochromocytomas/paragangliomas (10 benign, nine malignant). Eight out of 10 patients with benign tumours had positive MIBG scans. These were confined to the adrenal gland and the scan detected all known disease except for the contralateral adrenal gland in one patient with bilateral tumours. One patient with a negative scan had an adrenal tumour and the other one had an extra-adrenal (5 cm diameter para-aortic mass) tumour. Nine patients had metastatic phaeos with elevation of plasma or urinary catecholamines present in all. Five patients (all females) had positive scans and all known soft tissue lesions showed positive uptake. Three of these had extensive bony metastases and the extent of metastases was better demonstrated by ^{99}Tc^{m} scanning. In four (M:F 2:1) with metastatic disease, MIBG imaging did not show any uptake, three of whom had primary adrenal tumours and one tumour arising in the organ of Zuckerlandl. These patients had been referred for possible MIBG therapy. Our data suggest that MIBG uptake in malignant tumours is less common and that ^{99}Tc^{m} bone scanning is more sensitive in the detection of bony metastases. The loss of the ability to concentrate MIBG has been previously described during progressive disease and may reflect increasing tumour ded-ifferentiation. We are currently reviewing these patients further to see whether there are any other factors which may determine uptake of MIBG by malignant phaeos.

Renal biopsy: small or large calibre needle?

S. England, J. Rose, P. Geddy and R. Wilkinson
Departments of Radiology and Nephrology, Freeman Hospital, Newcastle Upon Tyne, NE7 7DN

Ultrasound imaging and sonar biopsy guidance has an established place in renal biopsy. Many different types of biopsy needle have been advocated for sonar guided procedures. The Biopty "gun" (Radiplast AB) is an automatic device with a cutting needle of 14 or 18 gauge size. The purpose of this prospective study was to determine whether an 18 gauge needle would be adequate for the histology of medical renal diseases and to assess the morbidity of renal biopsy. During a 15 month period 157 renal biopsies were randomly allocated to one of three study groups, including a control population (Menghini needle) and those biopsied with a 14 gauge or an 18 gauge Biopty needle. Kidney length, depth and internal features were recorded by ultrasound before biopsy. The number of passes made with each needle and the number of tissue cores obtained were noted. Each sample was analysed for size and for number of glomeruli. The results of this study, still in analysis, will probably show that for most purposes the 18 gauge Biopty needle was adequate. The major complications have occurred exclusively in the Menghini group.

Ultrasound-guided biopsy training using an agar phantom

K. A. Meakin, D. Killeen and P. C. Rowlands
Department of Radiology, Royal Liverpool Hospital, Liverpool L7 8XP

In the past radiologists have been trained in the performance of ultrasound-guided biopsy in patients. The technique can be difficult and distressing to patients and some skill is required to obtain diagnostic specimens. We describe a method of making an ultrasound phantom using blood agar containing suspended biopsy targets, and describe the effect of its use in teaching on biopsy performance. A group of volunteers with varying degrees of experience was instructed to biopsy a particular specimen before and after a period of training. A Biopty gun and a 5 MHz curvilinear probe were used. The length of time to obtain a specimen, the number of passes (maximum of three) and the length of the biopsy core were measured before and after training. Statistical analysis of the preliminary series demonstrated a significant increase in biopsy core length but no change in the time taken or the number of passes. The results in a larger group of subjects will be presented. The preliminary results demonstrate a useful and easy technique of ultrasound-guided biopsy training which does not involve the use of patients.

CT-guided biopsy of mass lesions in the abdomen and pelvis

T. S. Creasy and S. J. Golding
Regional CT Unit, Churchill Hospital, Oxford OX3 7LJ

CT-guided placement of either "cutting needles" for histology or "fine needles" for aspiration cytology, as appropriate, should theorectically allow accurate and safe biopsy of mass lesions in both the abdomen and the pelvis. A prospective study of patients referred for biopsy to the Oxford Regional CT Unit from 1982 has been performed to determine both the practicability of performing CT-guided biopsy, using a "cutting needle" wherever possible, and the incidence of associated complications. More than 100 patients have been studied to date and the results indicate the CT-guided biopsy with cutting needles is practical in the majority of patients, and can be used with confidence and minimal risk. In a minority of patients the anatomical site and relationship of surrounding structures precluded cutting needle biopsy; however, in most of these patients a positive cytological diagnosis was made with fine needle aspiration cytology.

Monday 29 April

Oncology (4.15–5.45)

Norfolk Room

High performance liquid chromatography analysis of amino acids in human urine as an aid to the detection of cancer

A. El-Sharkawi and *C. A. Wellington
*Oncology Department, Singleton Hospital, Swansea, and *Chemistry Department, University College, Swansea*

The purpose of the present study is to determine the concentration of urinary amino acids (using high performance liquid chromatography) in a series of 75 volunteers assumed to be free of tumours and 45 cancer patients in order to explore the possibility of finding, in terms of amino acid concentrations, possible tumour markers. To 32 cm^3 of 0.00556 mol/l dansyl chloride in acetonitrile 64 cm^3 of the urine sample was added and the mixture left at room temperature for 35 min for the dansyl derivatives to form. The latter were extracted with three successive portions of 10 cm^3 of pentane which were combined and the pentane removed on a rotary evaporator. The residue was dissolved in exactly 5 cm^3 of 30% methanol/70% lithium carbonate – HCl buffer and 25µl was injected through a Rheadyne valve and analysed on 15 cm x 4.6 internal diameter 5µ Hypersil ODS column with a mobile phase of 40% methanol and 60% water containing 0.008% triethylamine and 0.6% glacial acetic acid. The total concentrations of amino acids detected in the urine of the cancer patients were all in the range 30.8 – 98.8 nmol/cm^3 (mean 64.2 ± 19.8 nmol/cm^3), and those detected in volunteers ranged from 534.6 to 144.3 nmol/cm^3 (mean 966.0 ± 225.2 nmol/cm^3). Our results suggest that metabolic abnormalities exist in cancer patients. Very little has been reported on the possibility of exploiting this phenomenon as a tumour marker. We intend to do so in subsequent work.

The significance of the excretion of glutamine in patients with breast cancer, non-breast cancer and normal volunteers

A. El-Sharkawi and *C. A. Wellington
*Oncology Department, Singleton Hospital, Swansea, and *Chemistry Department, University College, Swansea*

Malignant disease is commonly accompanied by metabolic changes. These metabolic changes may take the form of abnormalities in protein metabolism. The overall effects of the protein metabolic changes must be reflected in the levels of amino acids in the body fluid. Very little has been reported on the possibility of exploiting this phenomenon as a tumour marker. We have measured the concentration level of glutamine in the urine of 75 healthy volunteers and 22 patients with breast cancer and 23 patients with cancer (excluding breast tumours) using the technique of high performance liquid chromatography. The mean (± SD) concentrations (nmol/cm^3) of glutamine in normal volunteers was 14.0 ± 3.1. In patients with cancer (excluding breast) it was 4.3 ± 2.4 and in patients with breast cancer it was found that this amino acid was absent (within the sensitivity of these analyses). These results imply that patients with cancer excrete less glutamine in their urine than normal individuals. What is more intersting in the present study is the absence of glutamine in the urine of patients with breast carcinoma. The possible use of glutamine as a tumour marker in breast carcinoma is under evaluation.

The inhibition of breast and ovarian cancers using an anitbody-targeted photosensitizer

J. W. Dawson, J. Morgan, H. Barr, F. Savage, A. J. MacRobert, C. Dean and P. B. Boulos
Departments of Surgery and Haematology, University College and Middlesex School of Medicine, London WC1E 6JJ

Photodynamic therapy has been used to treat cancer but is limited by poor selectivity of photosensitizer for tumour and cutaneous side-effects. The tumour localization and cytotoxicity of a photosensitizer conjugated to a monoclonal antibody (MAb) has been investigated *in vitro* and *in vivo* to determine whether this is a suitable technique for the elimination of micro deposits of cancer. The photosensitizer phthalocyanine was conjugated to the MAb ICR2, targeted against epithelial membrane antigen expressed on human breast and ovarian cell lines (MCF7 and OVCAR3). *In vitro* cytotoxicity was assessed by incubating cultured cells with conjugate or free photosensitizer and exposure to 18 J/cm^2 red light. Viable cells were quantified using the mono tetrazolium thiazolol reduction assay. Tumour specificity and uptake of the conjugate was assessed in a nude mouse xenograft model using quantitative photometric fluorescence analysis. *In vitro* cytoxicity of the conjugate was 1000 times greater than free phthalocyanine (90% cell-kill using conjugated phthalocyanine at 10^{9}M compared with free phthalocyanine at 10^6 M) in both cell lines. Immunoreactivity assessed by non-competitive binding assay was impaired by conjugation but uptake of conjugated photosensitizer *in vitro* and *in vivo* showed tumour:normal ratios of 1000:1 (conventional PDT achieves ratios of only 2:1). The conjugate was stable *in vivo* and *in vitro*, measured by high performance liquid. Targeting a photosensitizer and illumination at operation may eradicate mircroscopic deposits of cancer and improve local recurrence.

Monitoring patients with ovarian carcinoma: the relationship of serum CA125 to serial CT scanning

E. Moskovic, *E. Wiltshaw, *P. Blake and C. Parsons
*Department of Radiology and *Gynaecological Oncology Unit, Royal Marsden Hospital, Fulham Road, London SW3 6JJ*

The serial levels of the serum tumour marker CA125 were compared with the results of concurrent abdominopelvic CT scans throughout the clinical course of 65 patients undergoing treatment for advance epithelial ovarian carcinoma at this institution. 23 of these patients subsequently underwent a second laparotomy following chemotherapy and the pathological findings were correlated with the pre-operative results of both the serum CA125 levels and CT scan appearances in order to establish the relative accuracies of the tow tests in the diagnosis of residual disease. Initially, all patients had an elevated CA125 level (more than 400 units/ml) which fell to normal following treatment in all cases. 75% of patients showed continuing evidence of disease on CT grounds when both clinical examination and serum CA125 levels had normalized during or following treatment. Patients whose maximum response was PR on CT criteria relapsed faster than those achieving CR, showing CT to be a useful indicator of residual disease when the CA125 level had normalized after chemotherapy. Comparing the CT results and CA125 levels after second-look surgery in 23 patients showed CT to have a sensitivity of 50% with a specificity of 100%. Using these data, a protocol for monitoring patients undergoing treatment and follow-up for ovarian carcinoma is suggested.

Efficiency of non-conventional radiotherapy regimes in patients with III-stage cervix uteri cancer with unfavourable prognosis

E. E. Vishnevskaya and I. A. Kosenko
Department of Oncogynecology, Research Institute of Oncology and Medical Radiology, 223052 Minsk, p. o. Lesnoy-2, USSR

The object of this investigation was to make more effective the treatment of patients with III-stage cervix uteri cancer by development of new radiotherapy regimes. Treatment results are presented for two patient groups, in which peculiarities of local tumour spread do not allow radionuclide sources to be located adequately during intracavitary irradiation, as well as for patients weakened by tumour intoxication, anemia, or severe concomitant diseases. Some of the patients were treated by the conventional method (70 patients), whereas others were treated in accordance with one of four developed radiation regimes (190 patients). New regimes have different spatial and temporal dose distributions. Total doses, delivered to the primary tumour and to the zone of its anatomical growth, were about 70–80 Gy and were the same for all developed regimes. In addition, the TDF factor was 125–135 and CRE equals 2020–2034. Comparative efficiency evaluation of the different radiotherapy regimes for cervix uteri cancer with unfavourable prognosis allowed us to ascertain the the 3-year survival rate for patients treated in accordance with the new radiotherapy regimes is 24.5% higher ($p<0.05$) and the incidence of destructive irradiative injuries of the rectum and urinary bladder is twofold lower ($p<0.05$) in comparison with patients irradiated by the conventional method. The use of non-conventional radiotherapy allowed us to achieve better results for patients with III-stage cervix uteri cancer with unfavourable prognosis.

Invasive cervical carcinoma: high dose-rate brachytherapy following external irradiation: a retrospective analysis of complications and pattern of relapse

M. L. M. Lybeert, *W. L. J. van Putten, M. A. Crommelin, J. G. Ribot and W. Dries

*Catharina Ziekenhuis, Eindhoven, The Netherlands, and *Dr Daniel den Hoed Cancer Centre, Rotterdam, The Netherlands*

In the period 1975–1988, 129 patients with cervical cancer were treated with radiotherapy. The standard technique was a course of external beam irradiation to the pelvis delivered by a four-field box technique, followed by two or more brachytherapy applications given by means of a Cathetron R (TEM-Varian). The brachytherapy dose was guided by the tumour regression on the external irradiation. The treatment policy allowed a higher dose in the case of slow or non-responding tumours. 46 patients presented with a stage I or IIA, 43 patients with a stage IIB and 40 patients with stage III or IV tumours. The initial treatment protocol favoured high doses, given by both the external irradiation and the brachytherapy. As high complication rates became obvious, doses were gradually decreased. A wide range of doses was observed: external, 30 – 54 Gy; brachytherapy, 6.1 – 41.3 Gy; total, 46.1 – 77 Gy. Overall 10-year survival rates were rather low: stage I and IIA, 50%: IIB, 31%; III and IV, 31%. However, the 10-year relapse-free survival figures were comparable with those from other reports: stage I and IIA, 75%; IIB, 67%; III and IV, 39%. The main cause of death (39/74) was a loco-regional relapse, followed by distant metastasis (15), treatment related complications (eight), secondary cancers (three) and other causes (nine). A multivariate analysis with endpoint loco-regional control showed no evidence of a higher probability of control with either higher external, brachytherapy or total irradiation dose. When corrected for stage and histology, response on external irradiation proved to be an independent prognostic factor for loco-regional control ($p = 0.005$). An overall major complication rate of 19% was recorded. The risk of complications increased with age ($p = 0.02$) and brachytherapy dose ($p < 0.001$). The break-point seemed to be 13.5 Gy with few complications below this dose level. We therefore recommend a maximum dose level of 13.5 Gy if no mid-line shielding is used in the external irradiation fields.

Radiation dose related changes in lectin staining pattern in oral squamous cell carcinomas

V. N. Bhattathiri, P. Remani, P. Raveendran, A. Raveendran, T. Vijayakumar and M. Krishnan Nair

Regional Cancer Centre, Trivandrum, India 695011

Smears from the lesions of 15 patients with squamous cell carcinoma of the oral cavity were taken before radiotherapy and after various fractions of radiation. These were examined after staining with Jack fruit lectin conjugated with horse radish peroxidase. Before radiation 16 – 99% of the cells showed membrane staining, the average being 67%. In two thirds of the patients, more than 50% of cells showed lectin staining. In general the percentage of cells with lectin staining decreased with increasing doses of radiation. After doses of less then 12 Gy, the average dropped to 47%. Between 12 and 20 Gy this was 34% and after doses of more than 20 Gy it was 24%. This decrease was not uniform in all cases. In three cases less than 10% of the cells showed staining with doses even less than 12 Gy, whereas in four cases, even after doses of more than 20 Gy, staining was seen in more than 25% of the cells. Lectins bind to glycoprotein and glycolipids on the cell membrane which are integral to many functions of the cell. Considering the fact that radiation may produce cell membrane damage directly or indirectly, it is an exciting possibility that assessment of radiation induced changes in lectin staining might be useful as a predictor of radiosensitivity.

Radiotherapy for subglottic carcinoma (15 year review)

B. J. Haylock and G. P. Deutsch

The Sussex Radiotherapy and Oncology Centre, Royal Sussex County Hospital, Brighton, BN2 5BE

Between 1976 and 1990, 263 patients with laryngeal carcinoma were treated by one radiotherapist. 23 (8.7%) were subglottic in origin, the mean age was 67 (50 – 79) years, and the sex ratio 11 women to 12 men. UICC 1987 staging: T1 9 (39%); T2 4 (17%); T3 7 (31%); T4 3 (13%), only one case had cervical lymphadenopathy (4%). Radiotherapy was given, using small parallel opposed wedged fields, with an intended tumour dose of 66 Gy in 33 daily fractions (three cases were treated only palliatively). No mediastinal radiotherapy was used. Mean follow up was 67 (9 – 165) months. Actuarial analysis showed a 2 year overall survival of 69.3% (excluding intercurrent deaths 78.3%), and a 2 year disease free survival of 68.6%. Failure was due to persistent disease (5 pts: T4 2; T3 2; T2 1) or recurrence (2 pts: both T3, salvaged by surgery at 5 and 20 months). No patient developed clinical mediastinal relapse. These better than expected results in early disease support primary radiotherapy to the neck alone, avoiding conventional mediastinal radiotherapy. A national questionnaire asking 67 consultant otolaryngologists for perceived incidence, cure rate, and preferred mode of treatment (67% responded) confirmed our belief that surgeons had a pessimistic perception of the value of radiotherapy.

Hormonal cytoreduction for acute retention in prostatic carcinoma

J. H. Davies and R. J. Shearer
Department of Urology, St George's Hospital, Tooting, London SW17

Transurethral resection of the malignant prostate is associated with a significant mortality and morbidity and may lead to the early development of metastatic disease. Hormonal cytoreduction of the prostate can be achieved effectively by the use of the luteinizing hormone releasing hormone analogue goserelin acetate (Zoladex). We investigated the use of this agent in the non-operative management of patients with carcinoma of the prostate presenting with acute urinary retention. 15 patients, with an average age of 74 years (range 64 – 85), admitted in acute urinary retention with carcinoma of the prostate diagnosed on clinical examination and needle biopsy, were treated with goserelin acetate (3.6 mg) given subcutaneously. Needle biopsy results were available within 24 h. All patients were given cyproterone acetate 100 mg t.d.s. prior to , and following, goserelin injection. Patients were discharged with catheter *in situ* and readmitted for trial without catheter at the time of a further goserelin injection 4 weeks later. Those patients who failed to pass urine satisfactorily were recatheterized and readmitted for a further goserelin injection and trial of catheter. Transurethral resection was performed on those patients who failed a second trial. Nine patients (60%) successfully passed urine after removal of catheter, six patients at the first trial of catheter. The average duration of stay at first presentation was 3 days. Hormonal cytoreduction is an alternative method of management of patients with carcinoma of the prostate presenting with acute urinary retention. It has significant implications in the reduction of complications following prostatectomy, reduction of stay in hospital and increased availability of operating theatre time.

Duct morphometry: a prognostic indicator in prostatic carcinoma

S. Liu, P. D. Miller, C. Sowter, G. Slavin and R. S. Kirby
Departments of Urology and Histopathology, St Bartholomew's Hospital, London EC1A 7BE

The use of morphometric analysis as a prognostic test in prostatic carcinoma has been explored recently. Various factors (*e.g.* nuclear roundness factor, ellipticity factor) in nuclear morphometry of prostate cancer calls have beenincriminated as significant prognostic indicators. We studied the total duct area by architectural morphometry and applied this as a prognostic index in prostatic carcinoma. Three groups of 15 patients were randomly selected from the pathology computer registry and studied: (1) benign prostatic hypertrophy, (2) well differentiated prostatic carcinoma (Gleason grade 1 to 2), (3) poorly differentiated prostatic carcinoma (Gleason grade 4 to 5). Standard H & E stained prostatic tissues were analysed by the Kontron image processing system at low magnification. A preset analytic programme was installed to measure the total duct area in each field by automated summation. 10 sequential fields of each sample were analysed objectively. The total duct area was calculated per patient as the mean of the duct areas of 10 fields analysed. The total duct area index was significantly higher for Group 1 than for Groups 2 or 3, and Group 2 was higher than that for Group 3. There were good correlations between the index with disease progression and survival. The total duct area index measured by architectural morphometry correlated well with Gleason grade and prognosis from this study. Whether this is a more powerful predictor than other prognostic indices remains to by tested, and a prospective study based on this finding is being carried out.

Low dose 'hemi-body' radiotherapy for metastatic bone pain

J. Le Vay, C. Keen and F. McKinna
Departments of Radiotherapy and Oncology, Velindre Hospital, Whitchurch, Cardiff, CF4 7XL

'Hemi-body' radiotherapy is a well established technique for palliation of pain from widespread bony metastases in advanced cancer. In conventional doses (8 or 6 Gy), a response rate of around 80% is seen, but this is often accompanied by significant toxicity, especially with respect to nausea and vomiting, necessitating admission. It is also not possible to repeat the treatment safely. A pilot study has been started to investigate the response and toxicity to a "low dose" (4 Gy) technique of hemi-body radiotherapy. The aim is to produce effective palliation with less toxicity, allowing out-patient treatment. Because of the lower dosage, re-treatment should also be possible. The study is ongoing and to date eight patients have been treated. The response rate has been 50% at 24 h, with 83% of patients having good or excellent relief of pain by 1 week. Toxicity has been acceptable with only one patient suffering Grade III toxicity with respect to nausea and vomiting. If these early results are upheld this technique may prove to be a significant advance.

Reduction in diameter of human hairs following irradiation

V. K. Sieber, E. M. Sugden, C. J. Alcock and R. R. Belton
Departments of Radiobiology, Radiotherapy and Oncology and Radiation Physics, Churchill Hospital, Oxford, OX3 7LJ

The damage to growing hair produced by exposure to radiation could, if quantifiable, be exploited as an non-invasive regional biological dosemeter useful in radiation accidents. Studies in mouse and pig models have shown a dose dependent reduction in hair diameter following exposure to X-rays and gamma rays over the range 0.5 – 5.0 Gy. A pilot study has been undertaken to test such a system in Man using radiotherapy patients having single shots or a second fraction at least 5 days after the first. Growing hair was identified and obtained by initial shaving of a small area within the radiation field, and subsequent plucking of any hair which grew over a period of 5 days after irradiation. The minimum diameter along the shaft of a plucked hair was related to the cut end ("control"). The average percentage reduction in diameter for hairs from each field when related to dose over the range 2 – 14 Gy did show a dose related response. The magnitude of response was less than that demonstrated in mouse and pig. Further studies are underway to establish the nature of the dose – effect relationship on human hair diameter which appears to differ from that in mouse and pig.

Scanned focused ultrasound hyperthermia

C. C. Vernon, J. W. Hand and M. V. Prior
Hyperthermia Unit, MRC Cyclotron Unit, Hammersmith Hospital, London W12 0HS

The technology for hyperthermia of superficial malignancies has now advanced to such a degree that Phase III Trials are in progress addressing the question of whether the addition of hyperthermia to irradiation increases local control. However, if hyperthermia has a part to play in cancer treatment it is much more likely to be important in the treatment of more deep-seated pelvic tumours where an improvement in local control can truly translate into an improved survival. We have been investigating the use of a scanned foucused ultrasound system (Focus 6500, Lifetec) which has the potential to deliver hyperthermia selectively to tumours deep in the body (*i.e.* up to 8–9 cm from the surface). So far we have treated 17 patients with bulky superficial tumours in the breast and axilla, as well as rectal and gynaecological tumours. Only in three patients were the treatments technically unsuccessful. In the rest satisfactory thermal doses were achieved, and in general the treatments were tolerated well. Follow-up has been short but we have observed 1 CR and 1 progressive disease, and the rest have had either subjective and/or objective responsesd. We have seen no serious side-effects. Considering the advanced nature of these cases this is a very encouraging response and we intend to continue this work.

Immunotherapy effect of THX on certain parameters of cellular immunity in breast cancer patients during local radiation therapy

S. Vrbić and S. Filipović
Institute of Oncology, 18000 Nis, 48 Braće Taskovića, Yugoslavia

Postoperative radiation therapy makes cellular immunity disturbances in breast cancer patients more pronounced. Following certain cellular immunity parameters dynamism in patients with immunotherapy, compared with the control group, we tried to determine immunomodulatory effects of THX. Tumour markers (CEA, TPA, Ca-15-3) and other relevant clinical and laboratory parameters were followed too. Our first results show that THX: accelerates tempo of leukocyte and lymphocyte count recovery after radiation therapy; stimulates delayed type hypersensitivity reaction (DTH) recovery during and after radiation therapy; strongly stimulates T lymphocyte count recovery in patients with lowered starting values during and after radiation therapy. Our first results suggest that THX diminishes the degree of supression during and accelerates recovery of cellular immunity after radiation therapy. The normalization of tumour marker levels that we noticed may be of prognostic value.

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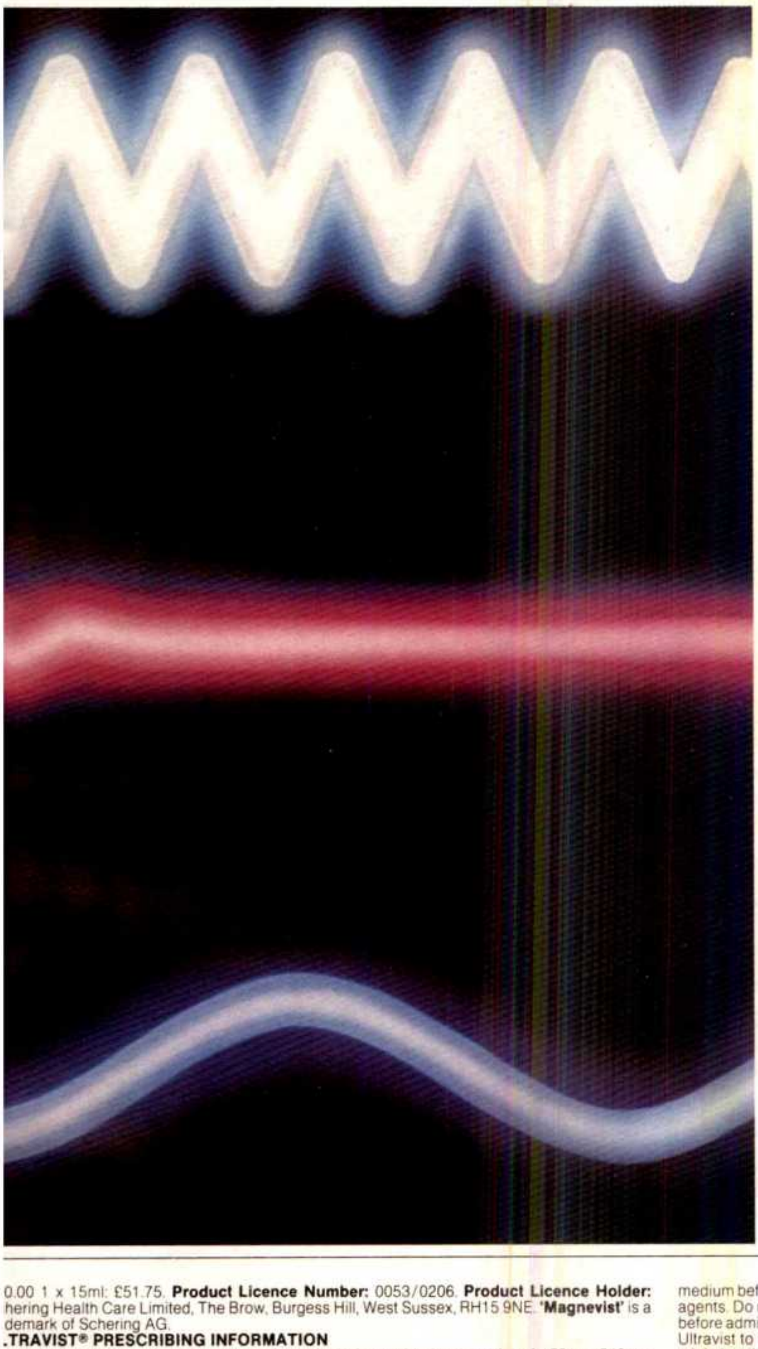

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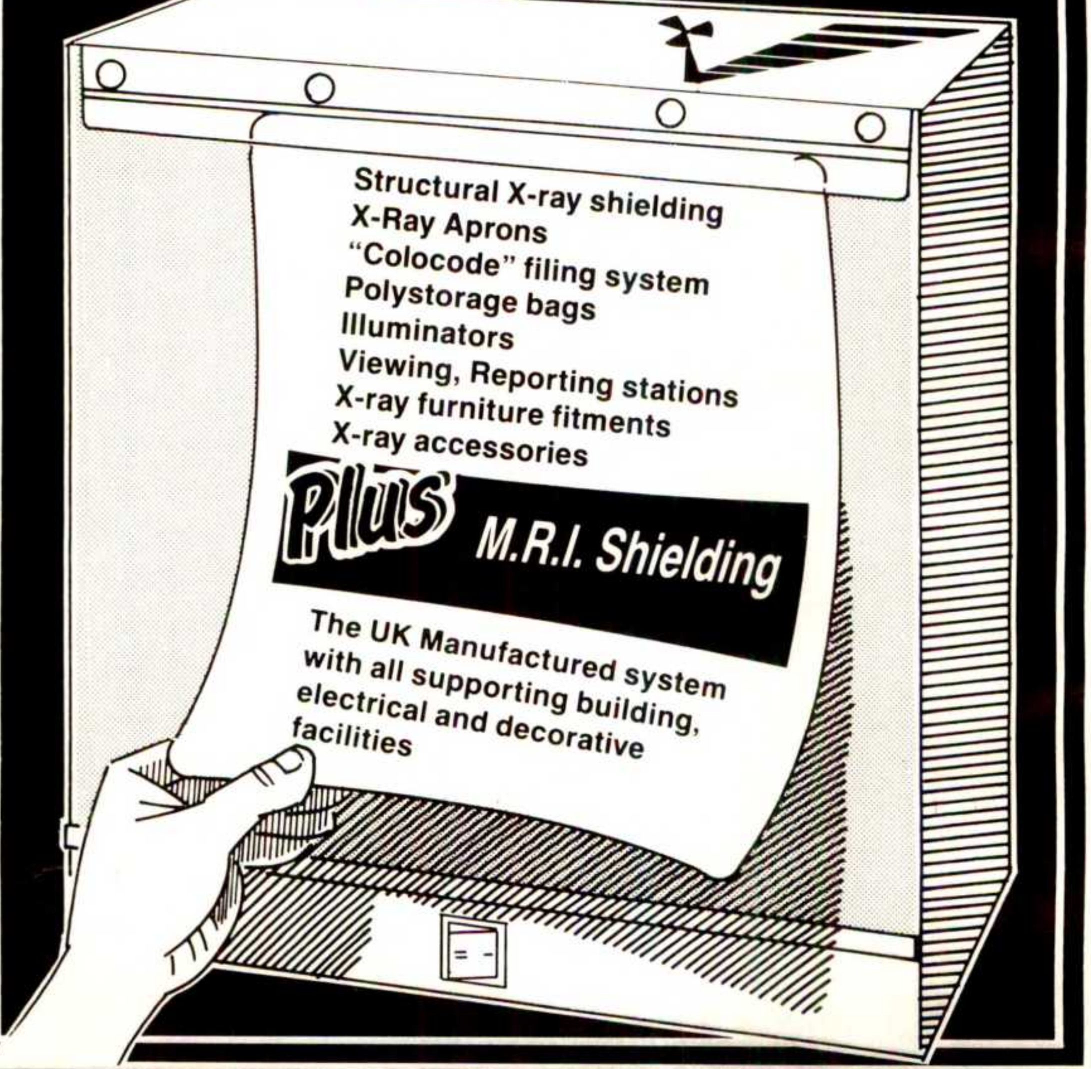

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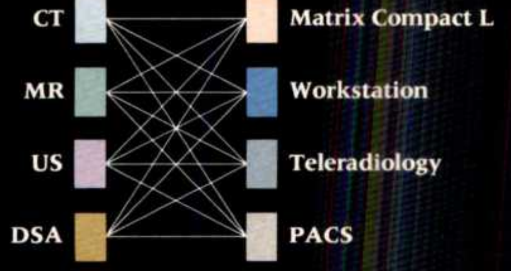

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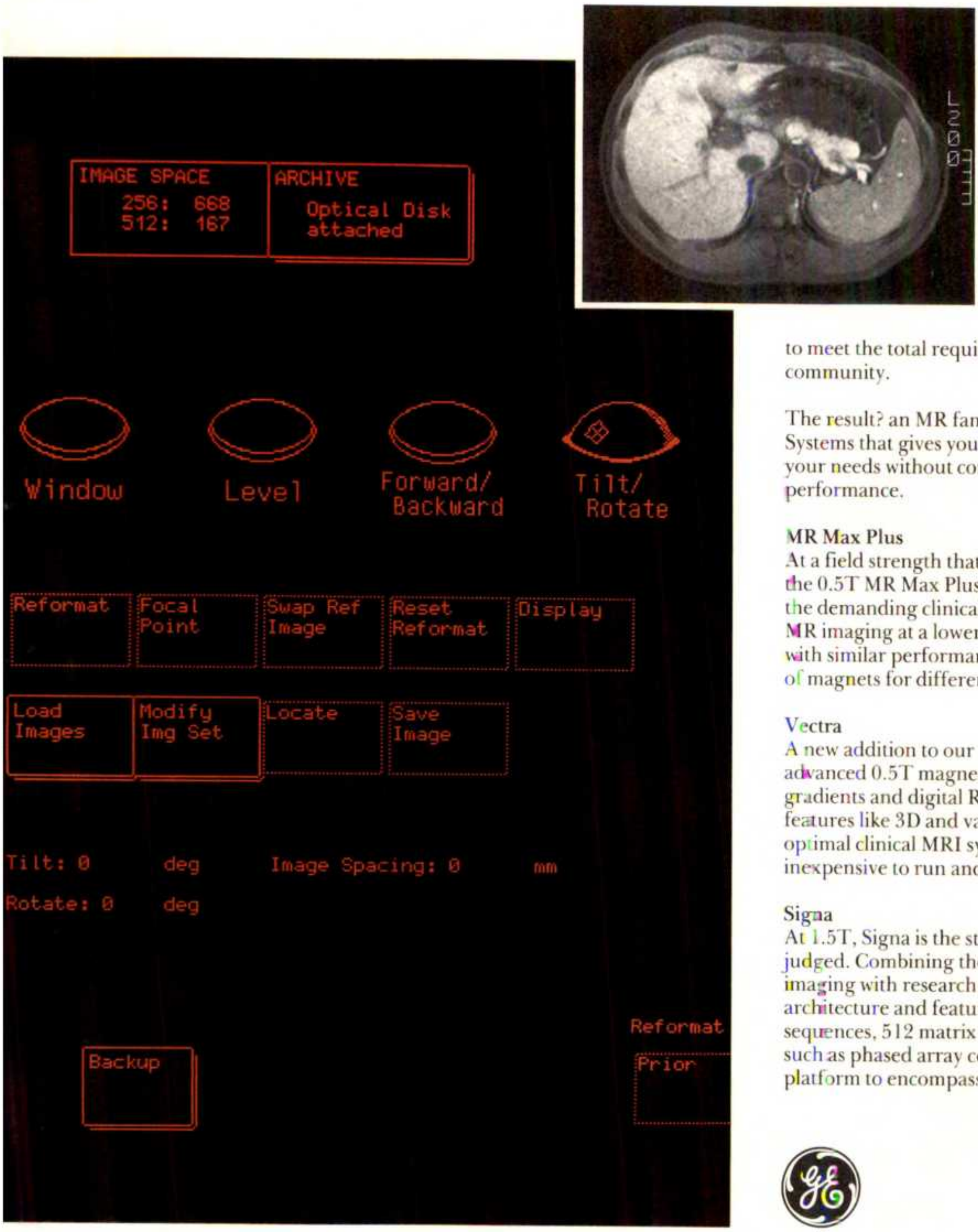

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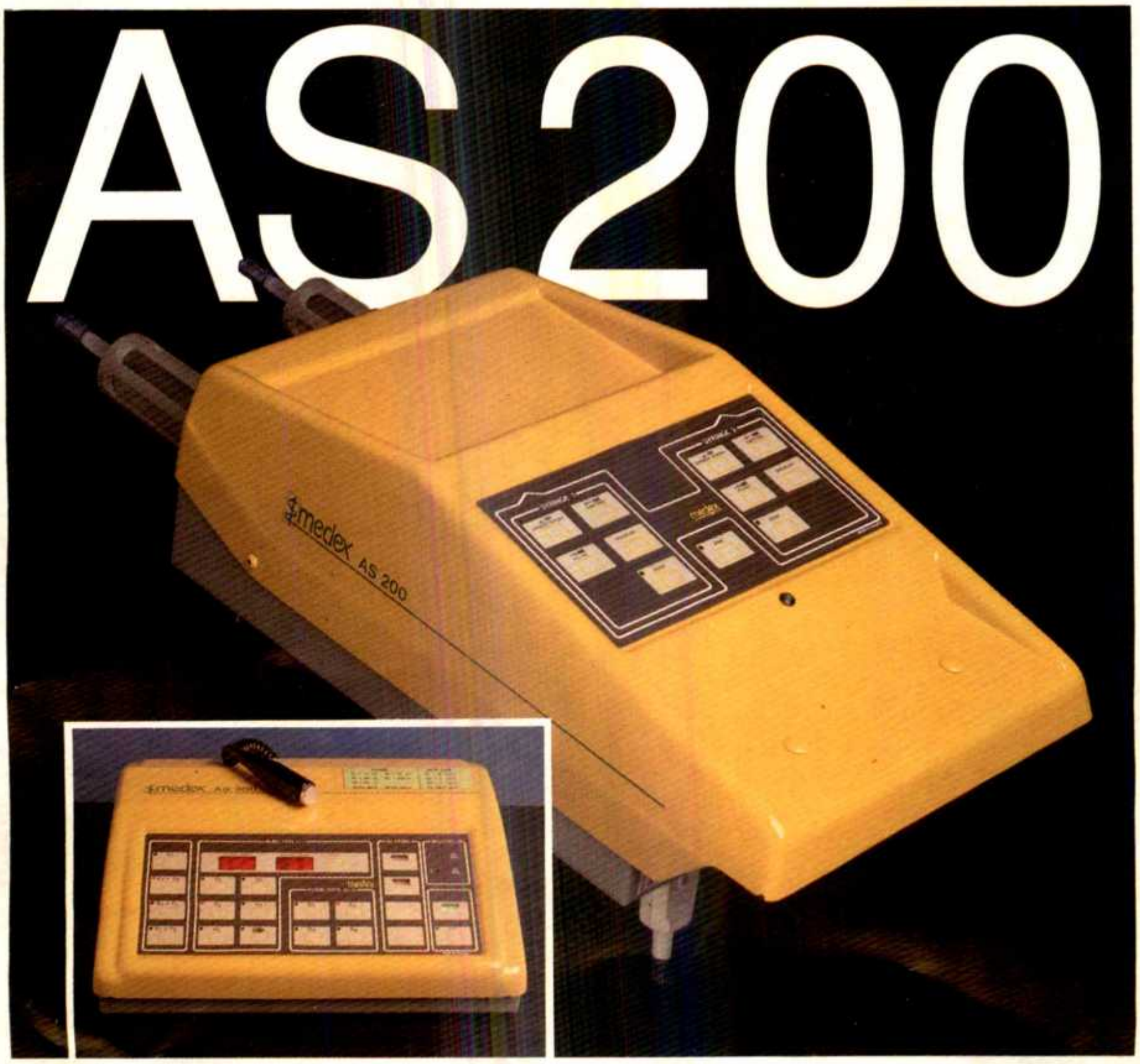

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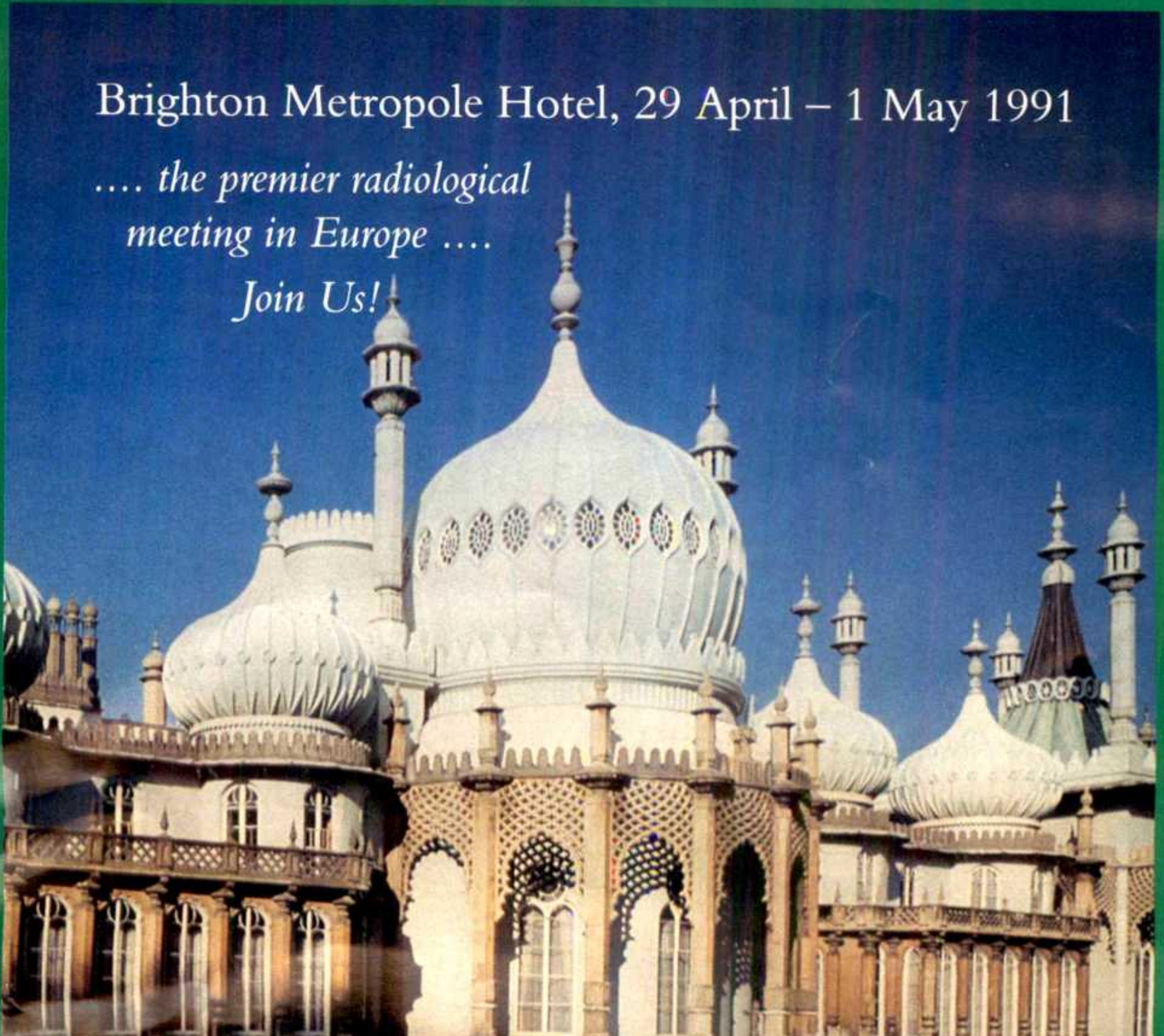

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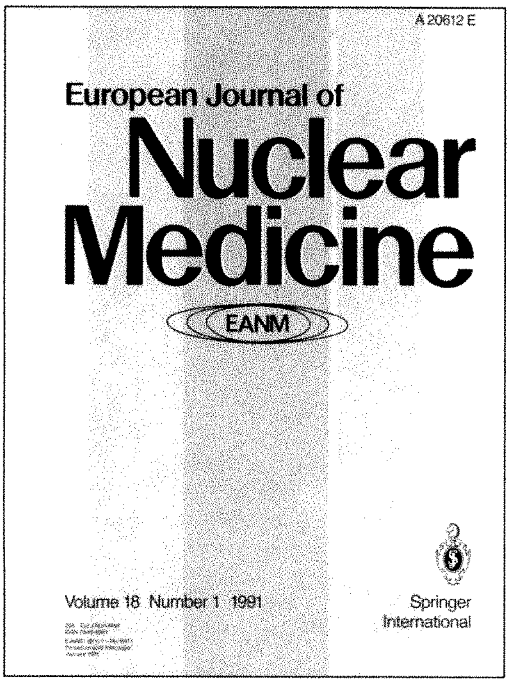

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"Neuro-Nuclear Medicine" 1990: what are the prospects?
G. Riccabona

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J. C. Buckland-Wright, D. G. Macfarlane, I. Fogelman, P. Emery, J. A. Lynch

Reproducibility of quantitative hexakis-2-methoxyisobutylisonitrile single photon emission tomography in stable coronary artery disease
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Editor:
E F J Ring, Royal National Hospital for Rheumatic Diseases, Bath, UK

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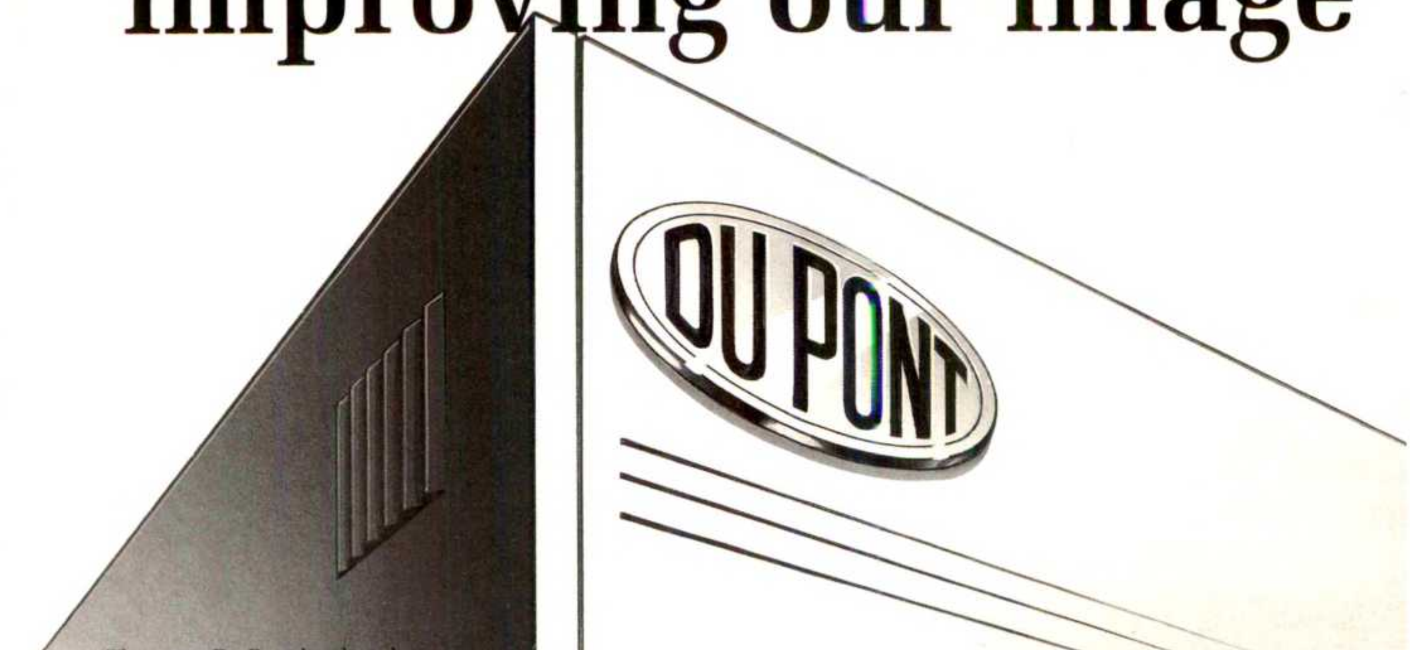

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Review article

Interventional ultrasound*

By H. H. Holm, MD, PhD

Ultrasound Department, Herlev Hospital, University of Copenhagen, DK-2730 Herlev, Denmark

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During recent years interventional ultrasound has become widely used and has had a great impact on patient management with regard to diagnosis as well as therapy. Many surgical procedures have been replaced by more gentle and less time-consuming "needle therapy" to the benefit of the patient.

Since material (in its broadest sense) can be removed from or deposited into the body under ultrasound guidance (for diagnostic and therapeutic purposes), "interventional ultrasound" includes a large number of different procedures. The first puncture transducer, which was based on the simple A-presentation principle, was described by Kratochwill in 1969 (personal communication). A few months later we performed abdominal needle biopsies guided by ultrasonic B-scanning using a "home-made" static scanner. The first punctures guided by dynamic scanning were performed using a linear array scanner with a puncture attachment (Pedersen, 1977). Today a large number of dedicated puncture transducers exist, as well as puncture attachments for abdominal scanners and transluminal transducers.

Principle

The scanner is moved until the target is seen on the monitor, then angled until the target is transected by the electronic puncture-line. A needle inserted through the needle-guiding device will now hit the target. A relatively strong needle tip echo indicates the position of the needle tip on its way to the target.

An alternative to this puncture method may be applied: a so-called "free hand" technique without the use of a needle guide. In this case, the needle may be introduced at a distance from the transducer, which need not necessarily be sterilized. A major drawback of the "free hand" technique is that it requires considerable skill and frequently repeated punctures unless the target is relatively large or superficially located.

The advantages of ultrasonically guided puncture are that it is rapid and convenient, dynamic images are provided, the needle is monitored during its insertion and varied puncture directions are possible. Furthermore, it is independent of organ function, no ionizing radiation is used, the equipment is mobile and the patient can stay in bed. Finally, the equipment is relatively inexpensive.

The limitations are that bone and gas are impermeable to ultrasound. This means that, for example, lung biopsies are usually impossible and punctures in patients with gas-filled gut may sometimes be difficult.

Diagnostic use

Guided diagnostic punctures for biopsy and aspiration are useful in many clinical settings.

Sophisticated imaging techniques, especially computed tomography (CT), magnetic resonance (MR) and ultrasound, make it possible to see more and smaller lesions that may represent malignancy. These methods, however, are generally non-specific and an additional fine needle biopsy is therefore often required.

In our institution, an ultrasonically guided fine needle biopsy is, in most cases, regarded as an integral part of the ultrasonic examination when an abdominal scan has revealed a lesion suspected of being a tumour whether in the liver, pancreas, kidney, gastrointestinal tract or the retroperitoneum.

Biopsy technique

There are many different biopsy techniques and needles. In our institution a 0.6 mm needle for cytological fine needle biopsy (CFNB), a 0.8 mm "Surecut" system for histological fine needle biopsy (HFNB) or a combination is used. An 18 gauge (1.2 mm) outer guide needle is always used for penetration of the abdominal wall.

To provide the necessary vacuum when the aspiration needle is moved up and down inside the target the needle is attached to a 10 cm^3 syringe which may be fitted with a special aspiration handle. Cytological material is expelled and smeared onto a glass slide (Holm & Kristensen, 1985).

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*Based on the Mackenzie Davidson Memorial Lecture given by Professor Holm at Radiology 90 in Harrogate, on 11 June 1990.

The "Surecut" needle is based on the Menghini principle. The needle, stylet and syringe form a single unit. The stylet is attached to the plunger of the syringe and, as the plunger is retracted, the stylet moves up in the needle revealing the cutting tip. A locking device retains the plunger in the retracted position, thereby maintaining the negative pressure when the needle is further advanced in the target area cutting out a tissue core. The needle is removed and the thin tissue core is expelled on a piece of sterile paper which then is cut and placed in formalin.

The two types of needles have almost the same outer diameter and they probably carry the same complication rate. The histological needle samples a smaller volume of the lesion and a slightly lower sensitivity is to be expected. The histological diagnosis is, on the other hand, more trustworthy since false positives theoretically do not occur. Furthermore, tumour typing is easier with histology.

The needle used depends on the type of patient and the target organ. If the patient has, for example, a known primary cancer and a lesion in the liver, a CFNB will suffice. The clinical problem is malignancy *versus* non-malignancy and the high sensitivity of CFNB is advantageous; tumour typing is not the issue.

If a patient without a known primary has a lesion in the liver, combined use of CFNB and HFNB is advantageous. Histological fine needle biopsy facilitates the search for the primary site. In such cases, an extra tissue core for electron microscopy may prove valuable. In any case, it is very important that the inverventionalist works in close collaboration with a skilled cytopathologist to achieve the optimum diagnostic information from the guided fine needle biopsies.

Coarse needle biopsies are usually taken using a Tru-cut type needle. The conventional Tru-cut needle must be manipulated using two hands and is therefore not well suited for biopsy under ultrasound guidance. It can, however, be most usefully mounted in various automated biopsy-gun systems. One such system is the so-called Biopty-system, which is expensive but highly effective. Special disposable Tru-cut type needles (gauge 14–20) are placed in the spring-loaded biopsy-gun which is then closed and ready for use. When the biopsy needle has been introduced up to the edge of the target area, the trigger is activated. The 26 mm long biopsy is rapidly taken and the system removed. Following a Biopty-type biopsy, the tract of the biopsy can be seen on the ultrasound image as an echogenic line confirming the position of the biopsy. The needle has to be removed from the gun to release the biopsy. This system can be used routinely for 1.2 mm prostatic biopsies and for large-core liver and kidney biopsies in non-neoplastic diffuse diseases.

Generally, there is a 1–2% false positive rate with cytological samples. There is not a significant false positive rate with microcore biopsies, but on the other hand these carry a 15% false negative rate as opposed to the 10% false negative rate with cytology. With both techniques insufficient material is obtained in 5% so that, with persistent clinical suspicion of malignancy, a number of repeated biopsies are necessary.

Preparation

Preparation of the patient before an ultrasound-guided interventional procedure depends on the nature of the investigation. In the case of a fine needle biopsy (*i.e.* external needle diameter below 1 mm) on a patient with no suspicion of a coagulation disorder, no laboratory test or other kind of preparation or post-puncture observation is required and the procedure can be performed on an outpatient basis. Thus the puncture is an integral part of the ultrasound study, and time is spared for both the patient and the department. However, if the patient's clinical condition or biochemical tests indicate a coagulation disorder, the procedure is only performed on inpatients and coagulation factors, thrombocyte counts and blood should be available.

Using the above fine needle policy means that, when clinicians refer patients with a suspected tumour to the ultrasound department, they can expect a morphological description the same day and a microscopic diagnosis 1 or 2 days later, providing a firm basis for diagnosis and treatment.

Biopsy of specific organs

The diagnosis of a pancreatic cancer can usually be based exclusively on ultrasonic scanning and an ultrasonically guided biopsy.

In case of renal masses, pre-operative evaluation routinely includes intravenous pyelograms, renograms, ultrasound plus an ultrasonically guided 0.8 mm Surecut biopsy. Aspiration cytology from the kidney has more or less been abolished, since it led to an unacceptable number of false positive results (5%). Ultrasound scanning is used for the detection of perirenal growth, lymph node enlargement and liver metastases as well as caval thrombosis. The biopsy may provide, pre-operatively, the important differentiation between a renal carcinoma and pelvic tumour, occasionally difficult with imaging alone. It may also aid in the diagnosis of benign conditions such as haemangiomyolipomas, oncocytomas, haematomas, etc.

Finally, solid focal lesions in the liver may represent a benign condition rather than liver metastases. Even in cases where the ultrasound scan is quite typical of liver metastases, most oncologists will require microscopic proof before chemotherapy.

Both CFNB and HFNB of the liver carry a high success rate. Furthermore, interpretation of the material is not difficult since the mere presence of extrahepatic cells or tissue indicates a tumour deposit, making cytological criteria of malignancy secondary. Only in cases of primary liver tumours are cytological criteria of malignancy crucial.

Biopsies from other organ systems may present problems. For example, in a series of 43 CFNB and HFNB from solid gynaecological masses each needle type provided sufficient material in approximately 80% of all cases (Larsen, 1989, personal communication).

However, when performed simultaneously, the success rate (the rate of at least one biopsy being sufficient) was elevated to 96%. The explanation for this is probably that soft tumours are easy to biopsy with CFNB (the tissue is easily dislodged into the needle), whereas it is difficult to cut a core. Hard tumours, for instance uterine or ovarian fibromyomas, give meagre cytological results but excellent cores.

Extra-abdominal biopsies

The success of percutaneous abdominal biopsy techniques has resulted in their use in several extra-abdominal areas.

In 1981 a new technique for precise transperineal needle placement in the prostate guided by transrectal scanning was described (Holm & Gammelgaard, 1981). With some modifications, the technique is now used extensively to detect early prostatic cancer.

Considerably improved image quality has allowed the detection of echo-poor lesions (which may represent cancer) especially in the peripheral zone of the prostate (Lee et al, 1989). However, it is important to stress that not all echo-poor lesions represent cancer. Some represent artefacts, small cysts, localized hyperplasia, prostatitis, etc. Guided biopsies are therefore important. It is often easiest to detect prostatic cancer by transverse scanning which allows for comparison between the two symmetrical lobes. The advantage of longitudinal guided biopsies is that the entire needle path can be seen.

In our institution we use a 7 MHz multiplane rectal scanner (Brüel & Kjaer, model 8551) with a built-in oblique puncture canal for transrectal punctures (which are less painful) in combination with an automatic biopsy system. This is excellent for the diagnosis and staging of prostatic cancer including non-palpable cases. Several biopsies are usually taken, often also from the capsular and pericapsular region, for diagnostic and staging purposes.

Another example is the non-palpable but ultrasonically visible small testicular tumour. Ultrasound examination with biopsy may be valuable in "high risk" testes such as patients with a tumour in the other testis, in infertile men or in cases of non-descendced testes, where early diagnosis of an otherwise non-detectable tumour may be obtained.

Ultrasound and ultrasound-guided biopsies are valuable in the evaluation of the axillary lymph nodes in patients with suspicion of regional relapse after mastectomy (Damgaard, 1989). In a prospective series of 60 women with symptoms related to the axilla (such as oedema in 42 and pain or neurological symptoms in 18) but without abnormal signs on palpation, ultrasound detected nodes in 12 cases. Guided biopsy contained malignant cells in nine (15%) patients who therefore had additional treatment. Benign conditions were found in three cases. No abnormal nodes were identified in the remaining 48 cases and none of the 51 patients without detectable recurrence had a verified relapse during the 1-year follow-up.

Finally, it is possible to verify the presence of a parathyroid adenoma by an ultrasound-guided fine needle aspiration cytology or parathyroid hormone determination, or by a histological Surecut biopsy, when ultrasound has disclosed an echo-poor lesion adjacent to the thyroid gland (Karstrup et al, 1988). This might be helpful in the surgical search for an adenoma and also provides the necessary basis for percutaneous destruction of such a lesion by alcohol injection (see later).

Diagnostic puncture of fluid collections

Fluid collections, either in the form of cysts or as free fluid between the organs, may be aspirated for primary diagnostic purposes under ultrasound guidance. However, the quality of ultrasound scans is so high today that the benign nature of, for example, a simple cyst in the kidney is so obvious that a diagnostic puncture of such a cyst is superfluous in most cases.

Free fluid collections are another matter, as the management of the patient may depend on the nature of the fluid. The macroscopic appearance and laboratory tests of the aspirated fluid will often reveal the presence or absence of blood, pus, urine or bile.

X-ray contrast media injections

The introduction of X-ray contrast media into various hollow structures is considerably facilitated using ultrasound guidance. For example, antegrade pyelography is easily performed via a thin needle or a thin catheter placed under ultrasound guidance in the renal pelvis. An ultrasonically guided "abscess-graphy" to monitor cavity size and disclose communication between an abscess cavity and a hollow organ is another example. Two other obvious uses of injecting contrast media through inserted catheters are ultrasonically guided transhepatic cholangiography (PTC) and ultrasonically guided percutaneous pancreatography. Rather than relying on the supposedly normal anatomy, it is advantageous to perform the PTC under ultrasound guidance. Consequently, only one puncture is usually needed. Furthermore, if only part of the intrahepatic bile duct system is dilated, selective PTC can be performed. Percutaneous injection of contrast medium directly into a pancreatic duct can easily be performed under ultrasound guidance (Makuuchi & Bandai, 1985). This technique can be very useful in patients in whom ERCP is impossible, or biopsy of a suspected pancreatic mass is negative, or the exact extent of a malignancy should be defined for surgical reasons.

Central venous catheters are frequently placed in critically ill patients to ensure an intravenous route for nutrition, to measure venous pressure, etc. However, the commonly used blind procedure is not always easy and serious complications are frequent *e.g.* pneumothorax, arterial puncture, venous perforation. Nielsen & Nolsøe have therefore developed an ultrasonically guided one-hand technique for placement of a central venous catheter over a guide-wire. In 75 consecutive cases, the method has now been used successfully 70 times, with only two insignificant complications (Nolsøe et al, 1989a).

Therapeutic use

Interventional ultrasound plays an increasingly important role as a therapeutic technique.

Nephrostomy

Only a few years ago access to an obstructed upper urinary tract was a serious matter which involved general anaesthesia and in uraemic patients carried a significant operative risk. Today ultrasonically guided nephrostomy (Pedersen et al, 1976) is a rapid procedure which is performed under local anaesthesia with wide indications. These include not only postrenal obstruction, possibly bilateral, but also endoscopic surgery for certain pelvic tumours, for selected pelvic-ureteric junction strictures and especially for renal stones; a procedure which certainly has not become superfluous because of the introduction of extracorporeal shockwave lithotripsy.

Different techniques for catheter placement can be used, *e.g.* a one-shot or pigtail catheter type, or a self-retaining ballon catheter or so-called "loop catheters".

Di Lelio (1989, Personal communication) has described the interesting new technique of circumvallating nephrocystostomy, which he has used in 12 patients with postrenal obstruction, in whom it was impossible to pass ureteric catheters. Subcutaneous connection of a nephrostomy tube to a suprapubic bladder catheter seems to give very encouraging results.

Cholecystostomy and gastrostomy

In patients with cholecystitis unfit for surgery, ultrasound-guided cholecystostomy with, for example, a 10 F balloon catheter can be a useful procedure, also allowing percutaneous stone removal. The safest puncture route is transhepatically into the gallbladder where it is adherent to the liver. Furthermore, in patients with gastric in- or outlet obstruction, ultrasound-guided gastrostomy can be performed.

Pancreatic cyst treatment

"Long-term" catheter drainage may be indicated in patients with pancreatic cysts that cannot be controlled by repeated punctures. Catheter drainage is most simply performed using the trocar technique and pigtail catheters. Aspirated material is sent for amylase determination and culture. The puncture route is typically transperitoneal, but a retroperitoneal or transgastric route can also be used. Success rates ranging from 70% to 90% have been reported; on average the drainage continued about 20 days, ranging from a few days to about 3 months (vanSonnenberg et al, 1989).

For treatment of pancreatic pseudocysts, Hancke (1989, Personal communication) has developed an elegant percutaneous internal gastrostomy technique based on the use of a small double pigtail catheter introduced under combined ultrasound and gastroscopy control. Forty-five patients have been treated with this technique, the large majority with good results.

Abscess treatment

Another group of patients where treatment options have changed fundamentally during the last 5–8 years are those with intra-abdominal abscesses, where guided puncture has replaced the conventional surgical treatment.

Percutaneous drainage is an efficient treatment of intra-abdominal abscesses whether located in the peritoneal space, for example periappendicular abscesses and gynaecological abscesses, in the liver or kidney or related to the pancreas, with guided puncture of the usually echo-poor lesion and, if overlying intestines can be avoided, insertion of a 14 gauge (1.9 mm) polyethylene catheter. Total aspiration of pus and careful irrigation with saline are performed until the returning fluid is clear (with repeated flushing of the catheter during the following days). Antibiotics may be injected but the efficacy of this has never been proven.

In a series of 180 intra-abdominal abscesses with variable bacteriology, we found comparable results whether repeated puncture or catheter drainage were used. Almost independent of the localization of the abscess, immediate clinical improvement and cure without surgery can be expected in 85% of cases using this procedure (Grønvall, 1985).

Pelvic abscesses, including those in relation to the lower genitourinary tract may be difficult to access transabdominally. A valuable alternative to the transabdominal route may be the transrectal, transvaginal or transperineal approach. Even large tubo-ovarian abscesses may be punctured and cured under transvaginal ultrasound guidance. A perirectal abscess may similarly be cured by one or more ultrasonically guided transperineal punctures.

Extra-abdominal abscesses, for example in the breast or located subcutaneously, can also be treated by this technique (Karstrup et al, 1991).

The most frequent use of ultrasound in the thorax is in determining whether a loculated pleural radiographic opacity is due to parenchymal consolidation or pleural effusion and to locate the best site for thoracocentesis.

Therapeutic application of material

The technique of ultrasonically guided application of material for therapeutic purposes was introduced in 1978, when vitamin-K was injected prophylactically under ultrasound control prenatally into the buttock of a fetus whose mother was undergoing anticoagulation treatment because of pulmonary embolism (Larsen et al, 1978).

Tissue destruction

Many new forms of ultrasound guided percutaneous therapy are currently being tested. In principle, there are at least three different means of tissue destruction applied through a needle: (1) chemical agents such as alcohol and antineoplastic drugs, (2) radioactivity in the form of interstitial placement of radioactive sources and (3) heat applied in the centre of a tumour using various tiny implantable energy sources like microwave antennas, coils and filaments.

Chemical parathyroidectomy

The ability to place a needle precisely in an often small parathyroid adenoma and obtain a reliable tissue diagnosis by means of hormone determination and fine needle histology has formed the basis of ultrasound-guided percutaneous inactivation of parathyroid tumours using intraglandular injection of 96% alcohol, so-called ultrasound-guided chemical parathyroidectomy. This procedure has been performed by Solbiati et al (1985) and by Karstrup et al (1987). The alcohol injections can be performed on an outpatient basis under local anaesthesia. The dose of alcohol is estimated individually, depending on the intraglandular dissemination. However, the dose should not exceed half the volume of the parathyroid tumour. The dissemination of the alcohol in the gland is assessed by the appearance of fine, dotted echoes spreading throughout the gland.

Thirty-one consecutive patients with HPT were treated according to a strict protocol. Eleven had to be excluded from the study: six because the parathyroid adenoma could not be seen. Among the remaining 20 patients, who were treated with up to three alcohol injections, two had to be excluded from the study: one because of a cardiac infarction and the other because of a recurrent laryngeal palsy. Among the remaining 18 patients, eight became normocalcaemic, in four there was a reduction but not correction of serum calcium and in six the serum calcium was unaltered (Karstrup et al, 1989).

Another series of 14 patients were later selected for this treatment either because of hypercalcaemic crisis, high surgical risk or refusal of surgery. Eleven became normocalcaemic, some with dramatic clinical results, *e.g.* a patient who after an unsuccessful neck exploration went into a severe hypercalcaemic crisis. Two alcohol injections saved the patient's life and a recurrent hypercalcaemic episode after 1½ years was treated successfully by a third alcohol injection (Karstrup et al, 1990).

On rare occasions this treatment caused vocal cord paralysis due to palsy of the recurrent laryngeal nerve. Three patients experienced temporary paralysis (up to 3 months) and in two cases damage was permanent but without subjective symptoms. Ultrasound-guided chemical parathyroidectomy is an attractive alternative to surgery. However, at present, such treatment is limited to patients with severe and life-threatening hypercalcaemia and to patients who are poor surgical candidates or refuse surgery.

Alcohol in liver lesions

A promising ultrasonically guided approach to the treatment of hepatocellular carcinoma (HCC) was introduced by Livraghi. The method, involving repeated alcohol injections in high-risk patients with focal lesions smaller than 5 cm, is now spreading in Italian, Japanese and other centres (Livraghi et al, 1988). Livraghi's material now consists of 23 patients with localized HCC smaller than 5 cm; 1–8 ml of alcohol were injected 1–2 times a week, up to a maximum of 12 times. No complications were encountered after 345 injections. All lesions decreased in size and showed necrotic material at FNB. Percutaneous alcohol injection is the first-line treatment for HCC less than 5 cm in surgical high-risk patients and seems to be an alternative to surgery in lesions less than 3 cm.

Coeliac plexus block

Alcohol may also be used for blocking the coeliac plexus and permanently relieving pain in patients with severe chronic upper abdominal pain (Gammelgaard & Jensen, 1980, Personal communication). On the basis of transverse and longitudinal ultrasound scans the location of the coeliac axis is determined. Under ultrasound guidance, a fine needle is placed as close as possible to each side of the origin of the coeliac axis. Coeliac ganglion neurolysis is performed by injection of 10 cm^3 96% alcohol on each side. Complete or almost complete pain relief can be obtained in a third of the patients. In another third there is pain reduction and in the remaining third no effect can be obtained by this technique. The treatment has proved to be less effective in chronic relapsing pancreatitis and ultrasonically guided plexus block should probably be reserved for chronic pain caused by pancreatic cancer.

Interstitial therapy

Interstitial therapy guided by ultrasonic scanning was introduced in 1981 by insertion of ^{125}I seeds in pancreatic cancer. The results were unsatisfactory (Frederic et al, 1991). Two years later a method for transperineal ^{125}I seed implantation in prostatic cancer guided by transrectal ultrasound scanning was developed (Holm et al, 1983), with implantation being performed through a multichannel puncture attachment mounted on a transrectal scanner producing transverse prostatic images. The minimal peripheral tumour dose was 160 Gy. In addition, 47 Gy of external irradiation was given, also covering the iliac nodes. The procedure turned out to be technically feasible and with very few early complications. However, the late results in the 32 patients were not impressive (Iversen et al, 1989). In 48% of the patients, guided biopsy still revealed cancer more than 1 year after the treatment. Furthermore, the late irradiation sequelae were unacceptable, since three patients had severe rectal complications and almost 50% had cystitis and proctitis. The implantation method proved to have one technical weakness, namely that the prostate was frequently displaced cephalad during the needle insertion sometimes leaving the proximal part of the gland uncovered by seeds. An improved implantation technique has been developed based on the use of a multiplane rectal scanner (Brüel & Kjaer, type 8551). The technique uses transverse as well as longitudinal scanning as a guide during the needle insertion. Very precise needle placement is thereby ensured (Holm et al, 1991).

In collaboration with Lee and co-workers in Ann Arbor, Michigan, a new method of treatment of prostatic cancer has been introduced based on the use of the implantation technique, using iridium in combination with hyperthermia. A number of thin catheters are inserted in the prostate. Microwave antennas are then inserted into the catheters for hyperthermia treatment. Then iridium seeds are temporarily inserted into the catheter to obtain precise radiation of the tumour and prostate, keeping a safe distance (1 cm) from the rectal wall. Finally, the hyperthermia is repeated for 1 hour. Eight patients have so far been treated without early complications. Time will show whether this treatment which, from a theoretical point of view, should be more efficient than irradiation alone, proves beneficial to the patients.

Laser treatment

Recently a new approach using a low power neodymium YAG laser as the energy source has been suggested (Nolsøe et al, 1989; Steger et al, 1989). Nd-YAG laser light may destroy tumour tissue by phototoxicity and thermoradiation. It can be applied directly into solid tissue since the light-conducting fibres can be introduced through a needle. It is therefore possible to combine interventional ultrasound with laser therapy. This demands two qualities of the laser fibre. Since most tumours are spherical, light should be emitted in a sphere and, in order to allow for a percutaneous technique, it should be possible to pass the fibre down the interior of a needle of limited diameter (*i.e.* below 18 gauge). A cone-shaped laser fibre tip which spreads the light and produces spherical lesions has recently been developed. The size of the lesions produced is dependent on the energy delivered by the system. The maximum diameter achieved was 44 mm (4 watts for 30 minutes were used). The lesions are characterized macroscopically by a central cavity delineated by a charred rim of tissue and, beyond this, a zone of coagulation. On ultrasound scanning the lesions appear as rounded hyperechoic areas. Using a purpose-built multi-canal needle steering device it is possible to place microthermocouples interstitially at known distances from the laser fibre tip. Temperature measurement and prediction of the approximate extent of thermodestruction are therefore possible. The findings suggest that ultrasound is a safe tool for monitoring the lesions produced by interstitial Nd-YAG laser hyperthermia.

After completion of a series of animal experiments (17 pigs' livers), treatment of liver metastases in three patients has been carried out without complications or technical problems (Nolsøe et al, 1990a). "Ultrasonically monitored percutaneous interstitial Nd-YAG laser hyperthermia" may become a technique for the future treatment of liver metastases, prostate cancer, parathyroid adenomas, CNS tumours and other distinctly demarcated neoplasms.

Complications

Complications are remarkably rare. At our institution we have, during the last 19 years, performed approximately 8000 ultrasound guided punctures, including 3500 fine needle aspiration biopsies for cytology and/or fine needle cutting biopsies for histological evaluation, using three passes with each needle. Seven hundred were large bore biopsies from kidneys, liver or prostate; 2800 were punctures of fluid collections and 1000 percutaneous nephrostomies using a pigtail catheter or a 10 F balloon catheter (Nolsøe et al, 1990b).

Only post-puncture conditions which required treatment were regarded as complications. Transient temperature rise, haematuria or pain which did not require treatment except analgesics and observation were not considered to be complications and consequently were not included. In the whole series we have noted a total of 15 complications of which three in patients with disseminated cancer were fatal. This gives an overall complication rate of 0.19% and a mortality rate of 0.04%. The fine needle data alone give similar results. Admittedly, these rates are minimum estimates, since our data are based upon feedback from the clinical departments. However, it is our experience that any complication is immediately reported.

Three out of seven complications were intraperitoneal bleeding in patients who had enlarged livers caused by multiple metastases, and the only death after fine needle biopsy occurred in this group. Based on this experience we have changed our guidelines so that patients with enlarged liver resulting from multiple metastases are considered to be at increased risk of bleeding and will not be biopsied routinely and without preparation.

Our fine needle mortality rate is in the same low order of magnitude as in three other published series (Gebel et al, 1986; Bret et al, 1988; Weis et al, 1988).

Although earlier experimental experience (Main & Dunning, 1946; Engzell et al, 1971) and clinical experience (Robbins et al, 1954; von Schreeb et al, 1967; Nordenström & Björk, 1973) show that fine needle biopsy of malignant tumours carries no risk of tumour seeding, more recent reports seem to demonstrate that tumour seeding (especially in conjunction with pancreatic biopsies) can occur (Ferrucci et al, 1979; Burlefinger et al, 1985; Bergenfeldt et al, 1988).

However, in our own material of 3500 fine needle biopsies with six needle passes per patient, we have never observed needle tract seeding, clinically or at subsequent surgery or autopsy.

Conclusions

The conclusions are that interventional ultrasound is an extremely valuable diagnostic and therapeutic tool sparing patients more traumatic procedures; that patient management today in many cases rests on a much firmer basis than before its introduction; that the future undoubtedly will bring many totally new applications of the technique; and that it, like any other procedure, carries a risk which, however, is remarkably low.

References

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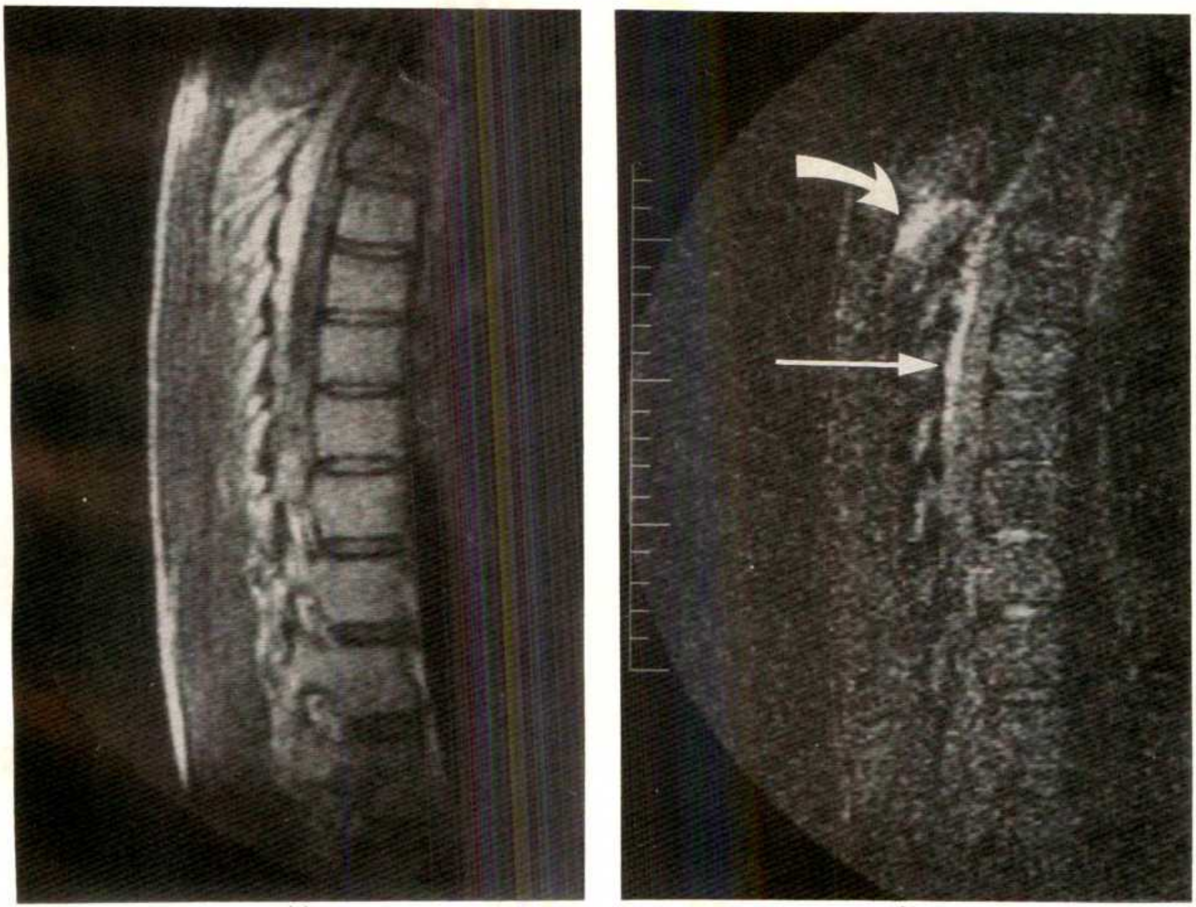
Table II. Proportion of examinations showing abnormalities in region

Region	Group 1 ($n = 44$)	Group 2 ($n = 74$)
Extraspinal	21 (48%)	2 (3%)
Vertebral column	27 (61%)	59 (79%)
Intraspinal	28 (63%)	38 (51%)
Normal	7 (16%)	11 (15%)

Group 1

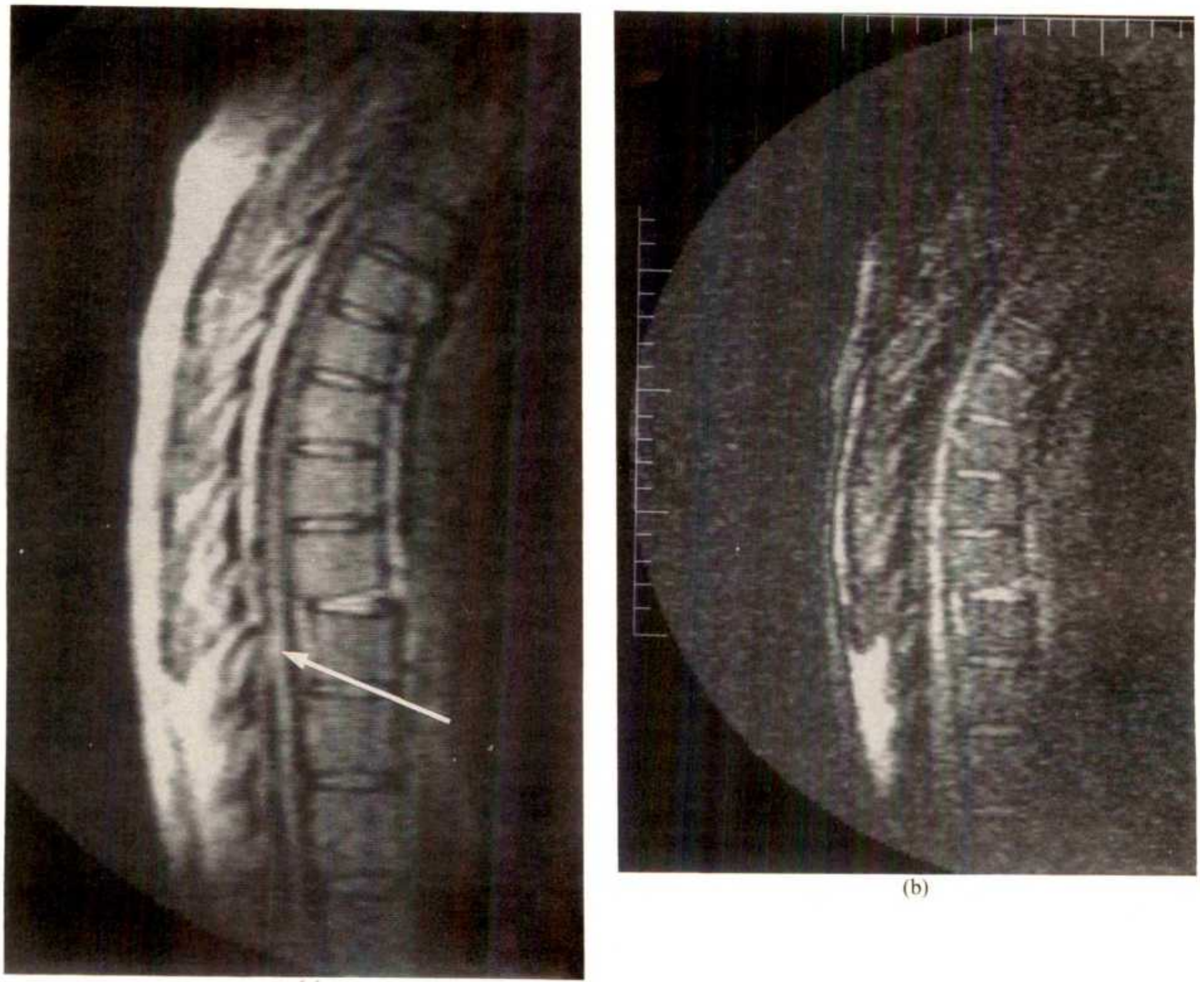
Of the 44 examinations, 10 were obtained within 24 hours of injury and 34 within the first week. Image quality was judged to be good or excellent in 68%, fair or poor in 30% and non-diagnostic in 2%. No abnormality was present in seven examinations (16%). Extraspinal soft tissue abnormalities were shown in 21 scans (48%) and comprised prevertebral soft tissue thickening and/or posterior ligamentous complex abnormalities. These were not seen later than 6 weeks after injury in any case. Prevertebral soft tissue thickening was shown in 7 cases (16%) and in each case was accompanied by a vertebral body fracture or fracture dislocation. The soft tissue thickening was visible on T_1WSE but was more conspicuous when STIR sequences were used where it was invariably of intense high signal intensity. Pathological confirmation of the nature of this material was not obtained in any case, but it probably represents haemorrhage and oedema.

Posterior ligamentous complex changes were seen in 19 cases (43%). These could often be appreciated on T_1WSE or T_2WSE images, when areas of high signal intensity corresponding to the location of the interspinous and intertransverse ligaments were shown, but were optimally demonstrated using a STIR sequence when the signal from intermuscular fat planes was suppressed (Fig. 1). Abnormal signal intensities in the posterior ligamentous complexes were accompanied by either vertebral column or intraspinal lesions in every



(a) (b)

Figure 1. Sagittal SE 500/40 (a) and STIR (b) images obtained 3 hours after injury (flexion-compression fracture of T4 with cord compression). Posterior ligamentous disruption (curved arrow) and acute extradural haematoma T1 and T7 (arrow) are best appreciated on STIR images.



(a)

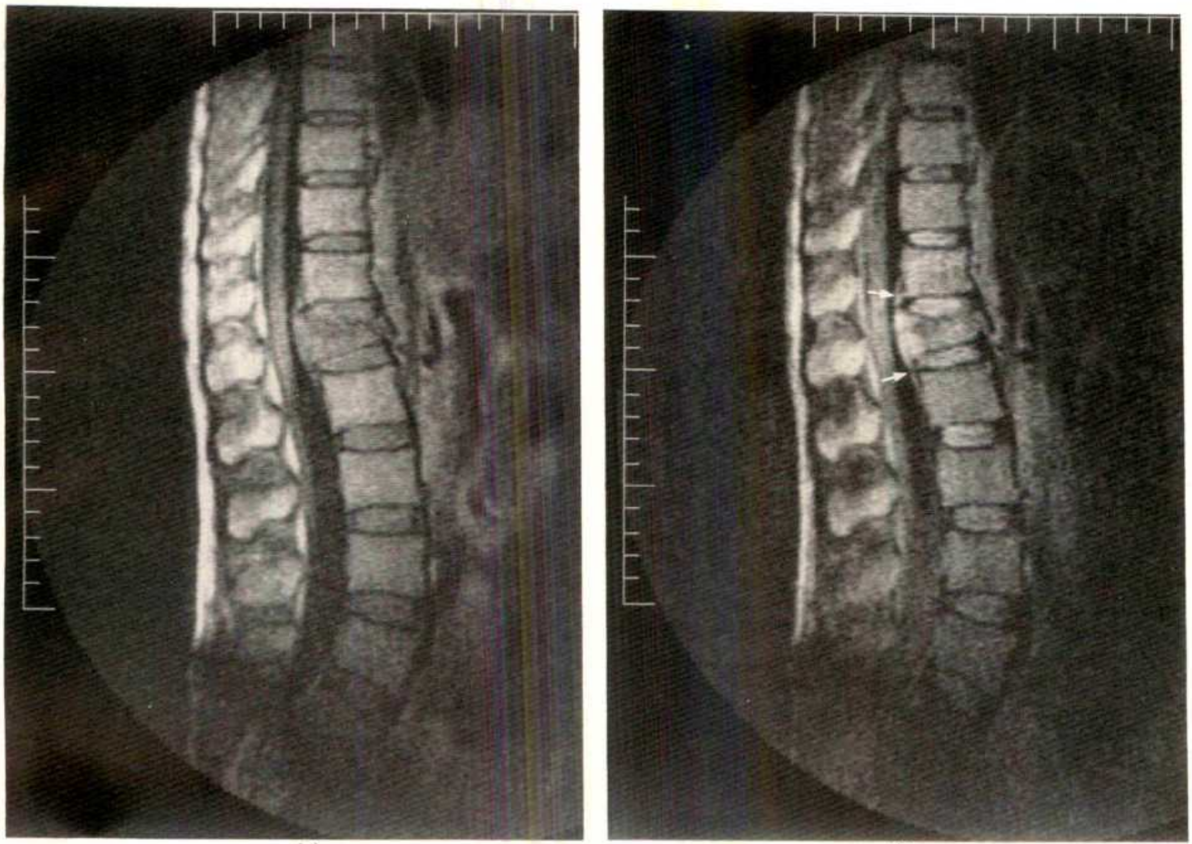
(b)

Figure 2. Sagittal SE 1600/80 (a) and STIR (b) images at 24 hours of a "Chance" type fracture at T8/9. High signal intensity changes extend from the prevertebral tissues into the widened disc space, anteriorly within the canal and involve the posterior ligamentous complex. Changes consistent with cord contusion are seen on the T_2WSE (arrow).

case, and may be considered a marker of more severe injuries. However, intraspinal abnormalities were present in seven cases where no extraspinal soft tissue changes were seen. In five of these, a STIR sequence was not used whilst in the remaining two cases, where a STIR sequence had been used, the additional findings were of traumatic disc protrusions causing cord displacement or compression. In four scans, high signal intensity changes were shown running between the prevertebral soft tissues, through the disc at the level of injury and into the posterior ligamentous complex, possibly representing the tissues which had sustained the greatest stresses at the time of injury. These were seen in one "Chance" fracture (Fig. 2), one fracture dislocation and two burst fractures.

The anterior longitudinal ligament (ALL) appeared disrupted in five cases (four burst fractures of L1, one horizontal shearing type injury in the lower thoracic region). Disruption of the posterior longitudinal ligament (PLL) was not seen in any case, probably because of the lack of contrast between the low signal intensity PLL, the low signal intensity cerebro-spinal fluid (CSF) and the low signal intensity posterior cortical bone on T_1WSE: gradient echo techniques which highlight the CSF pool would clearly be helpful in this context.

Vertebral column abnormalities were present in 27 examinations, of whom only two showed no overt lesion in the extraspinal soft tissues or intraspinal contents. Vertebral body fractures, shown by loss of normal vertebral body contour or alteration of signal intensity (Fig. 3), were the commonest finding (18 cases) while fractures of the posterior neural arch were diagnosed in two cases. Alteration of vertebral body signal intensity was shown in nine cases (increased signal on T_2WSE or STIR in eight, reduced in one). Focal canal stenosis was present in 17 cases and, in seven of these,



(a) (b)

Figure 3. Sagittal SE 500/40 (a) and SE 1660/80 (b) images at 3 days after injury (burst fracture of L1 with moderate canal stenosis but no spinal cord injury). Note the loss of marrow signal anteriorly in L1 body on T_1WSE (a) and high signal posteriorly on T_2WSE. There is preservation of disc morphology and signal intensity. The PLL is elevated but intact (arrow).

disc protrusions contributed to focal canal narrowing. These cases are detailed in Table III.

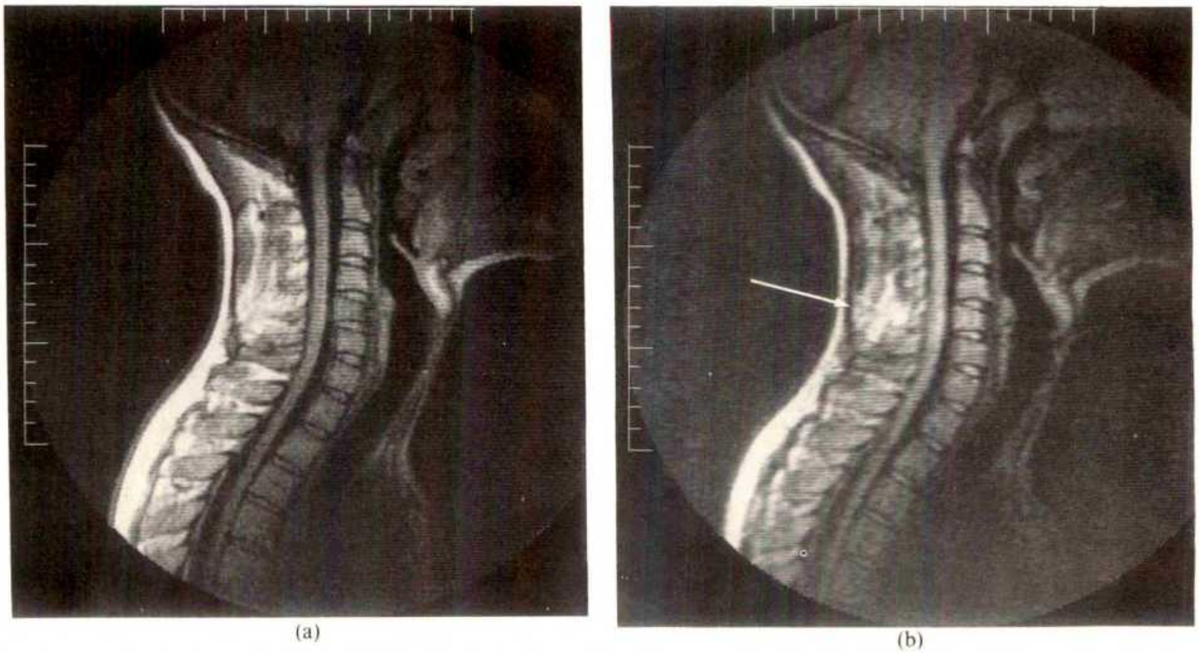
Disc protrusion was documented in seven out of 23 patients (30%) with recent cervical trauma. Spinal cord changes (contusion or compression) were present in all but one of these cases, though the degree of cord compression did not warrant decompressive surgery in any. Most of these patients were of ages such that coincidental disc protrusions or spondylotic changes would be uncommon. More severe disc injuries, such as complete disruption, shown by loss of continuity of the superior or inferior disc margins were seen in only three cases. In each of these, reduced signal intensity of central disc material was shown on either T_2WSE or STIR sequences along with clear loss of margination of the affected disc. Two were thoracolumbar and one a cervical injury.

Intraspinal abnormalities were present in 28 scans (64%), some showing more than one abnormality. These included extradural haematoma in 17, cord

Table III. Acute traumatic disc protrusions: level and intraspinal changes

Case	1	2	3	4	5	6	7
Age, years	22	26	39	55	35	42	50
Level	C3/4	C2/3	C3/4	C6/7	C3/4	C2/3	C4/5
Cord compression	−	+	+	−	−	+	+
Cord contusion	+	+	−	+	−	−	−
Extradural Haematoma	+	−	−	−	+	+	−

Key: + feature present, − feature absent.



(a) (b)

Figure 4. Sagittal SE 500/40 (a) and SE 1600/80 (b) images obtained 24 hours after axial loading injury. The cord morphology is normal (a), but there is high signal intensity anteriorly within the cord at C5 (b). Note the anterior compression of the body of C5 and high signal changes posteriorly in the interspinous ligaments (arrow).

compression or displacement in 15 and cord contusion in 11. Acute extradural haematomas were of intermediate to high signal intensity on all pulse sequences, but were most obvious when a STIR sequence was used. This was particularly true for examinations in the thoracic region where the presence of variable amounts of posteriorly situated extradural fat could cause diagnostic confusion (see Fig. 1). In two of the more recent cases, the presence of extradural haematoma was confirmed surgically; both of these were patients with incomplete neurological deficits examined within a few hours of injury. Magnetic resonance imaging allowed diagnosis and localization of an extradural haematoma, demonstrated the extent of cord compression and guided the surgical approach. In the remaining cases, pathological confirmation was not obtained; in one, a follow-up examination 10 days later showed resolution of the haematoma. In 12 examinations, the haematomas were localized around the injury site, involving one or two spinal segments, and in five cases were diffuse, involving three to seven, (mean five) segments. Vertebral column injuries were present in all but three of these cases, one of which was associated with an obstetric epidural anaesthetic. Extradural haematoma was responsible for cord compression or displacement in four cases and contributed to cord compression in a further six cases. Cord compression due to bone fragments was present in seven examinations and due to disc protrusion in four. In each case, the relationships of the spinal cord and theca to the cause of compression could be readily ascertained.

Changes consistent with spinal cord contusion were present in 11 cases. The spinal cord was of normal morphology in eight cases, focally enlarged in two cases and more diffusely swollen in one case. The cord was of normal signal intensity on T_1WSE, except in three cases, two of which demonstrated minimal hyperintensity and one focal hypointensity. Typically T_2WSE showed hyperintensity, particularly anteriorly within the spinal cord (Fig. 4). The exceptions were a single case in which spinal cord hyperintensity was only shown on a STIR sequence and a further single case in which a central area of slightly reduced signal intensity was present on T_2WSE with surrounding hyperintensity (Fig. 5). The changes were confined to the level of injury in all except one case which showed abnormalities extending over three spinal segments (Fig. 6). Additional abnormalities such as extraspinal soft tissue injury, extradural haematoma or vertebral body fractures were present in the majority of instances (see Fig. 6).

Group 2

Scan quality was judged to be good or excellent in 78%, fair or poor in 20% and non-diagnostic in 2%. Eleven (15%) of the scans were entirely normal. Changes in the extra-spinal soft tissues, with regions of high signal intensity in the posterior ligamentous complex were shown in two cases. Both examinations were obtained within 6 weeks of injury and these changes were best shown using the STIR sequence.

The vertebral column was normal in 15 cases; of these, changes in the spinal cord were shown in five

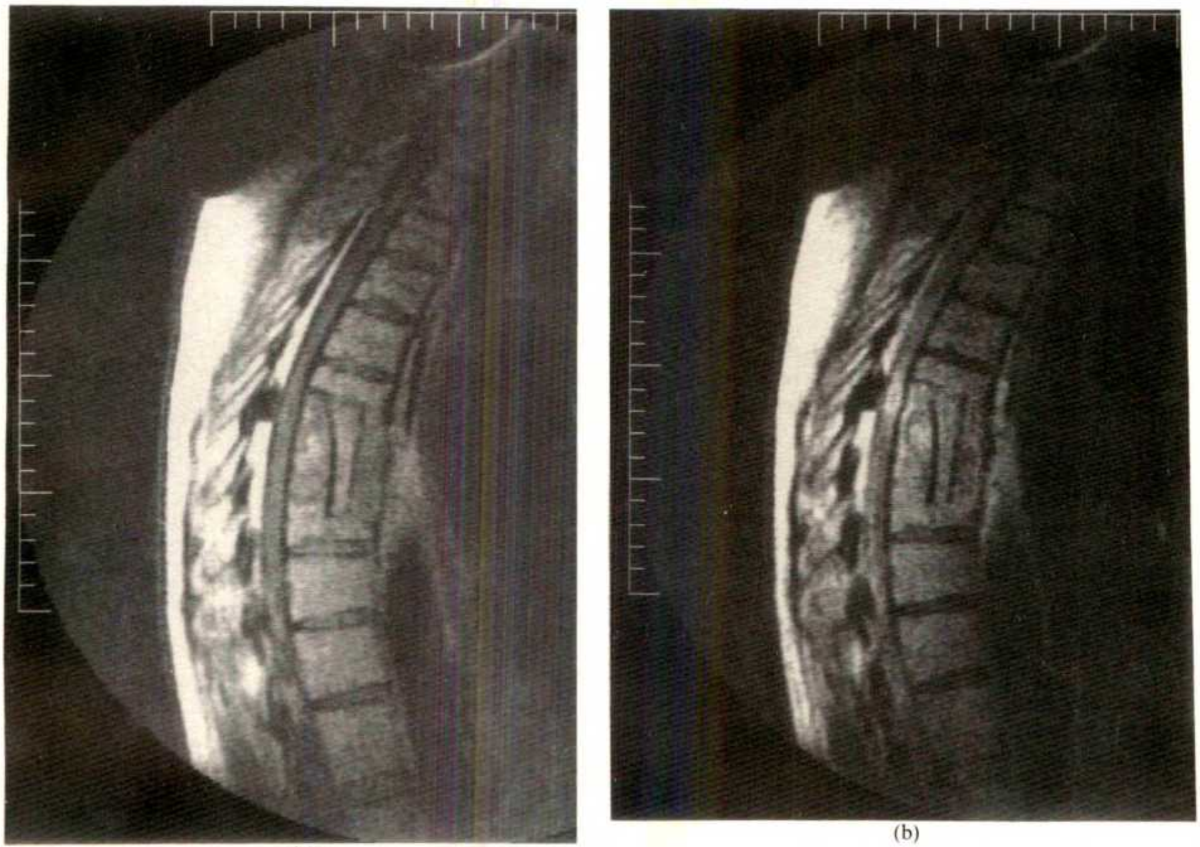


Figure 5. Sagittal SE 500/40 (a) and SE 1600/80 (b) images obtained 7 days after anterior decompression for herniated thoracic disc. Note the slight focal cord swelling and hypointensity in (a). In (b), central hypointensity and peripheral hyperintensity is shown, suggesting resolving haemorrhagic contusion.

cases (atrophy two, cystic myelomalacia two and a syrinx in one, the latter occurring following a stab wound). Abnormalities of the vertebral column or intervertebral discs were present in 59 (79%) of examinations. The changes shown included fractures of the vertebral body (49 scans), focal bony canal stenosis (21 scans), altered vertebral body signal intensity (six scans) and vertical vertebral body cleft (six scans). The development of a vertical vertebral body cleft over a 1-year period was documented in a single case in which MRI in the acute phase demonstrated endplate fractures and abnormal vertebral body signal intensity.

Disc protrusions were present, either as an isolated feature or in association with bony changes, in 16 scans. These were associated with spinal cord abnormalities in 11 scans (compression, six; atrophy, two; syrinx, two; contusion, one). Abnormalities of disc height or signal intensity were shown in 25 cases. Two patterns were seen. The first was that of loss of disc height accompanied by loss of signal intesity on T_2WSE at the level of fracture-dislocations (usually cervico-thoracic). Secondly, the disc above the level of thoracolumbar burst fractures showed loss of height and signal intensity while the disc below the level of these fractures was usually normal (Fig. 7). Where a vertical vertebral body cleft had developed, disc material herniated into the vertebral body defect, mainly from the disc above, though without loss of signal intensity.

Intraspinal abnormalities were shown in 38 (51%). Spinal cord compression or displacement was present in 17 cases, due to bony narrowing in 11 cases and disc protrusion in six (Fig. 8). Atrophy of the spinal cord was shown in 13 cases, not being seen earlier than 4 months following trauma. These changes were maximal at the site of injury and involved between three and 11 spinal segments, mean 5.7 segments (Fig. 9). High signal changes (T_1WSE) were seen within the cord on four of these scans. The features of myelomalacia (focal moderately well defined high signal intensity on T_2WSE with or without small punctate regions of low signal intensity on T_1WSE) were present in eight cases. These changes were shown at the level of previous injury and were not seen earlier than 6 months post-trauma (Fig. 10). They were usually, but not invariably, accompanied by other

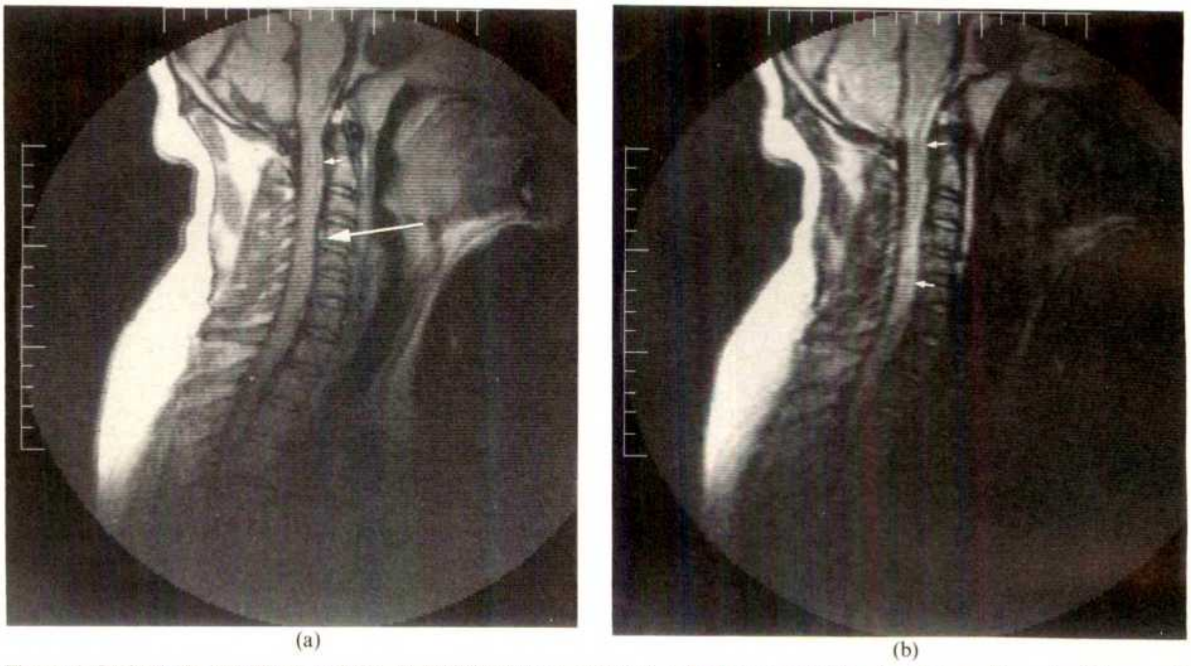


Figure 6. Sagittal SE 500/40 (a) and SE 1600/80 (b) images obtained following an axial loading injury. There is diffuse cord swelling between C2 and C7, with hyperintensity anteriorly at C4/5 on T_2WSE (b). There is a traumatic protrusion of the C4/5 disc with craniad migration (straight arrow) and extensive anterior epidural haematoma (short arrows).

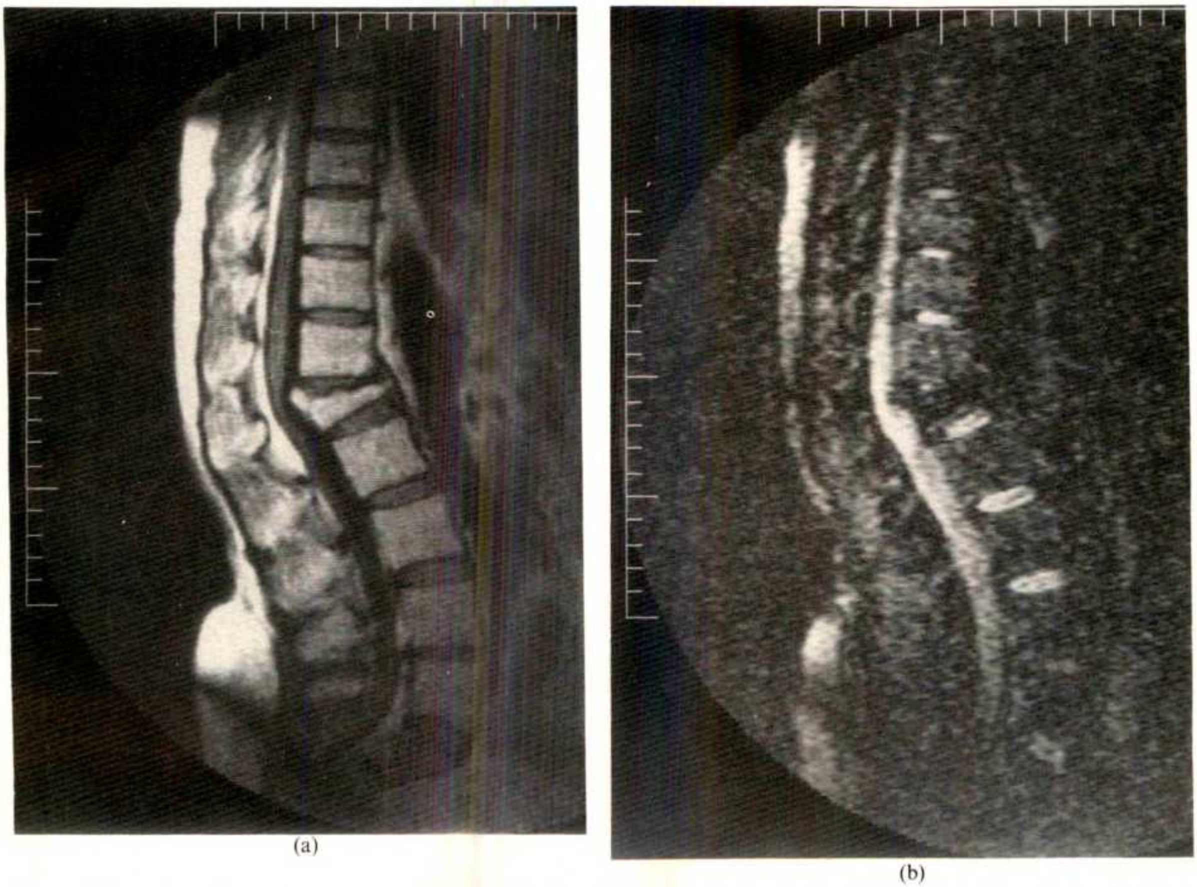
intraspinal abnormalities (cord compression or atrophy) and vertebral column abnormalities were present in all but two of these cases. In a single case, previous therapeutic transection of the cord was confirmed; the absence of residual syringohydromyelia was established by MRI. Spinal cord tethering at the site of injury was shown in only one case, a cervical fracture-dislocation in which the cord was atrophic but surrounded by strands of intermediate signal intensity and intimately apposed to the posterior thecal sac. Tethering may have been present in other cases where the cord was apposed to the thecal sac but other factors such as the presence of canal stenosis or cord displacement by bone or disc did not permit positive identification of an abnormal cord position due to tethering.

Syringohydromyelia was present in 10 patients, and was not seen earlier than 6 months following trauma. All were well defined regions of low signal intensity within the cord substance on T_1WSE and involved between 3 and 20 spinal segments. In four of six cervical and upper thoracic injuries the size of the cavity above the level of injury was considerably greater than that below the level of injury (Fig. 11). Focal canal stenosis of 44–60% was present in these cases and the cord was noted to occupy the entire width of the spinal canal at the level of injury. Typically, the spinal cord was enlarged, the syrinx appeared distended and contained multiple fibroglial bands or septations above the level of injury, while below, it was smooth walled and the syrinx appeared partially collapsed with only minimal spinal cord expansion (Fig. 12). A similar but less consistent pattern of abnormalities was seen with the thoracolumbar injuries in which a syrinx had developed. In one case, there was considerable expansion of the lumbar theca below the level of a previous L1 burst fracture in which the conus, expanded by a distended syrinx, appeared to be causing a ball-valve type obstruction to cephalad CSF flow (Fig. 13).

Discussion

Spinal trauma is a common and devastating event with important long term sequelae for both the individual and society. Neurological deficits may be transient, incomplete or complete. Patients with an incomplete deficit may benefit from aggressive therapy aimed at limiting secondary deterioration due to spinal cord ischaemia and compression consequent upon treatable causes such as disc herniation or extradural haematoma. Management is best provided in dedicated spinal injury units (Johnston, 1989). It is in patients with incomplete neurological deficits that MR imaging in the acute phase offers the most potential practical benefit. Particular advantages of MRI are the ability to monitor changes non-invasively within the spinal cord in both the short and longer term in an attempt to identify predictors of outcome and better understand the natural history of post-traumatic spinal cord syndromes.

Classification of spinal trauma into acute and chronic categories is somewhat arbitrary. During the first week of spinal cord injury, most of the metabolic derange-


(a)

(b)

Figure 7. Images of a burst fracture of L1, 3 years after injury. There is moderate canal stenosis and the conus is displaced posteriorly (a: SE 500/40). Note the loss of height and signal intensity of T12/L1 disc on STIR images (b).

ments, vascular changes and oedema will have already occurred. The subacute and chronic changes subsequently evolve, but there are no clinical or radiological markers that permit their separation. Injury to the bony spine can be considered acute if it has occurred within 3 weeks, as during this period most fractures behave like fresh fractures and may be reduced by conventional distraction devices (Quencer, 1988).

Magnetic resonance imaging in patients who have sustained spinal trauma allows direct visualization of the extraspinal soft tissues, the vertebral column and the intraspinal contents in a manner that has not previously been possible. While conventional radiography remains of paramount importance, MR imaging is capable of providing information of critical importance in determining patient management strategies in both acute (Goldberg et al, 1988; Mirvis et al, 1988a; Quencer, 1988) and chronic (Quencer et al, 1986; MacDonald et al, 1988; Quencer, 1988) spinal injuries.

Technical considerations

Magnetic resonance imaging in medically unstable patients remains difficult, though not impossible, particularly at low field strengths. Cervical traction devices using metal weights and tongs may be temporarily removed in some cases (cervical dislocation without fracture or posterior element fracture only) or replaced by an MRI-compatible system using water bags (McArdle et al, 1986) in cases where traction should be maintained (vertebral body fractures with retropulsed bone fragments which have been reduced by traction) (Quencer, 1988). Traction devices may cause difficulties with surface coil placement and induction of eddy currents causing either local artefacts or heating effects, especially at high field (Kanal et al, 1990). Use of titanium rather than stainless steel wire for internal fixation may be of advantage in reducing local image degradation (Mirvis et al, 1988b). We experienced one case in which a C1/2 fracture-dislocation could not be imaged owing to artefacts from a halo traction device (though a second clinically unsuspected high thoracic injury was revealed). In a single case, the presence of Luque rods resulted in a non-diagnostic examination.

Truncation artefacts, which may mimic the appearances of syringohydromyelia, cause artefactual central low signal intensity within the cord (Czervionke et al,

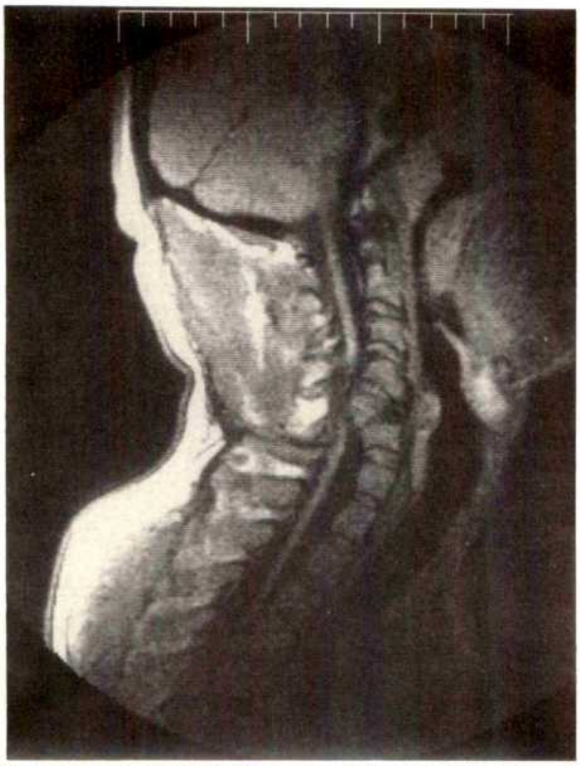


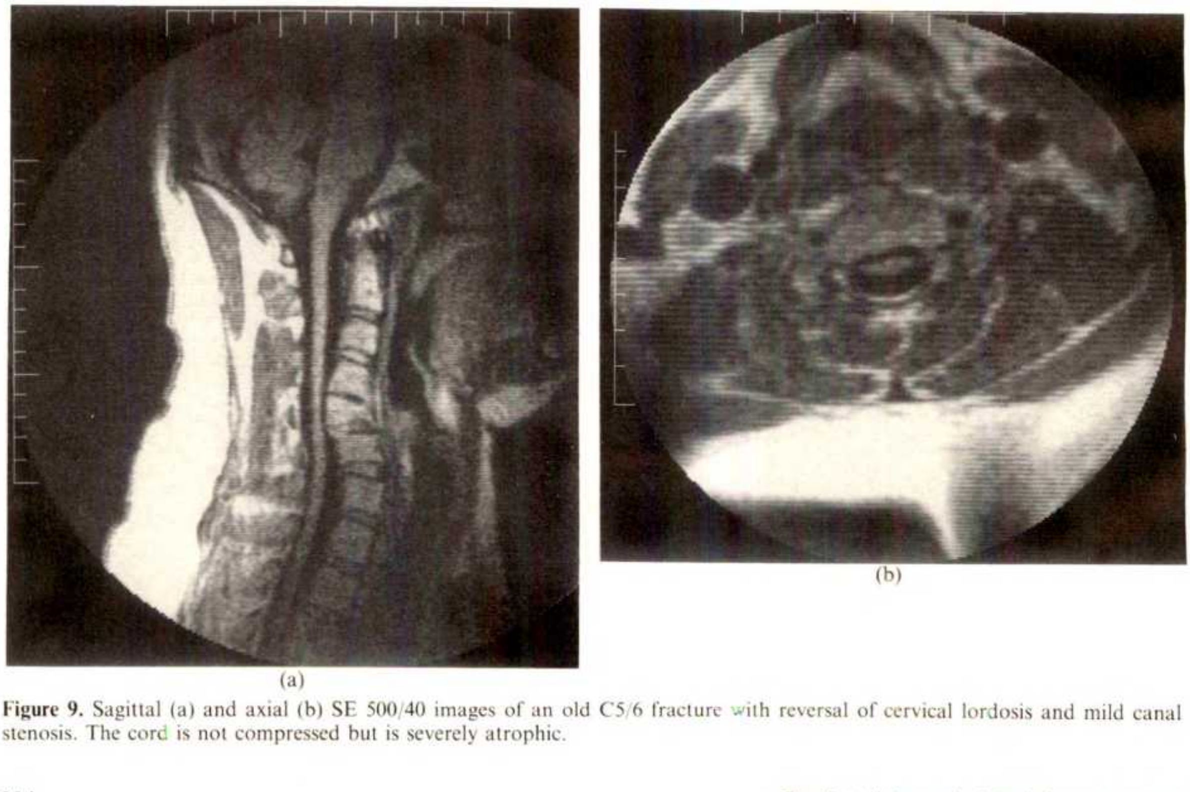
Figure 8. Sagittal SE 500/40 image of fracture-dislocation of C5, 4 years after injury. There is severe focal canal stenosis and malalignment in the mid-cervical region. The spinal cord remains compressed and markedly atrophic.

1988) or overestimation of cord atrophy (Yousem et al, 1990). These may be minimized by reduction of pixel size by either decreasing the field of view or increasing matrix size to 256 × 256 or greater (Czervionke et al, 1988). In our experience, the use of both sagittal and axial imaging planes is also crucial to the accurate assessment of cord morphology and signal characteristics, and helps to differentiate artefact from pathological cord changes.

Operation at low field (0.15T) has advantages in limiting some artefacts, but at the cost of relatively poor spatial resolution, signal to noise ratio and minimum slice thickness. Use of phase-sensitive techniques would be an advantage in evaluating spinal cord tethering and CSF dynamics. With current spatial resolution, computed tomography (CT) myelography is still required for the assessment of post-traumatic radiculopathy and brachial plexus injuries.

Vertebral column

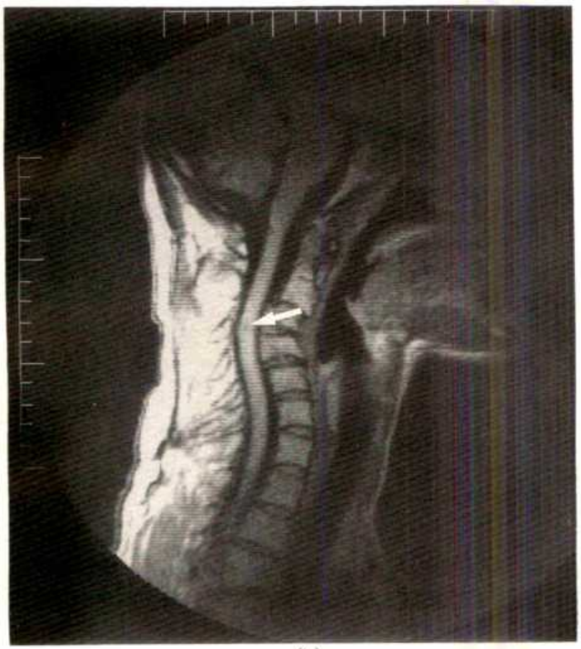
Plain radiographs remain the mainstay of initial assessment of skeletal injury. In comparison with conventional radiographs, CT has been shown to be more sensitive in the detection of neural arch fractures and more accurate in assessing spinal canal and lateral recess narrowing (Lynch et al, 1986). The ability to diagnose stable fractures positively which may be treated by early mobilization or conversely to show indirect evidence of ligamentous disruption requiring open surgery are two further advantages of CT over



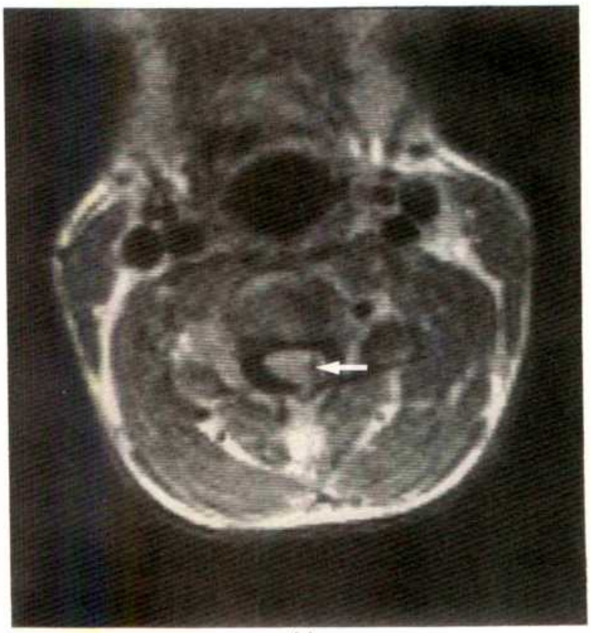
(a)

(b)

Figure 9. Sagittal (a) and axial (b) SE 500/40 images of an old C5/6 fracture with reversal of cervical lordosis and mild canal stenosis. The cord is not compressed but is severely atrophic.

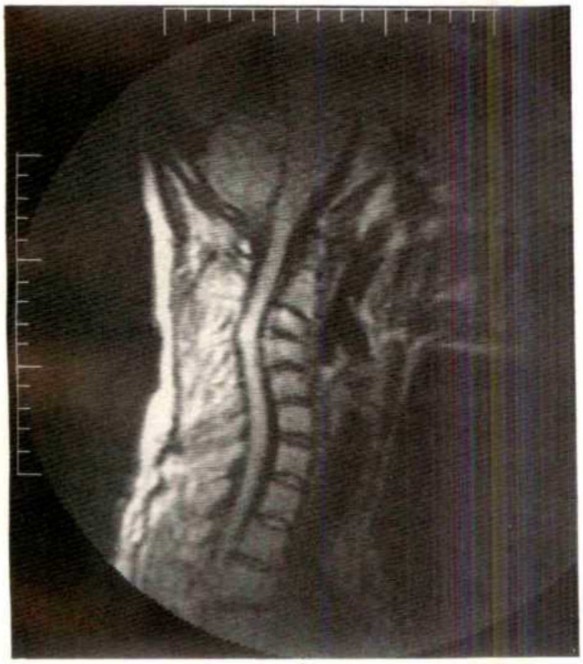


(a)



(c)

Figure 10. Sagittal SE 500/40 (a), SE 1600/80 (b) and axial SE 500/40 (c) images of cystic myelomalacia, 6 months after injury. Hyperintensity within cord on T_2WSE (b) and poorly defined hypointense foci on T_1WSE (arrows).



(b)

conventional radiography. However, assessment of longitudinally orientated structures such as the odontoid peg remains limited, even if reformatted images are obtained and evaluation of long segments of the spine is time-consuming and involves a significant radiation dose. Magnetic resonance imaging offers profound

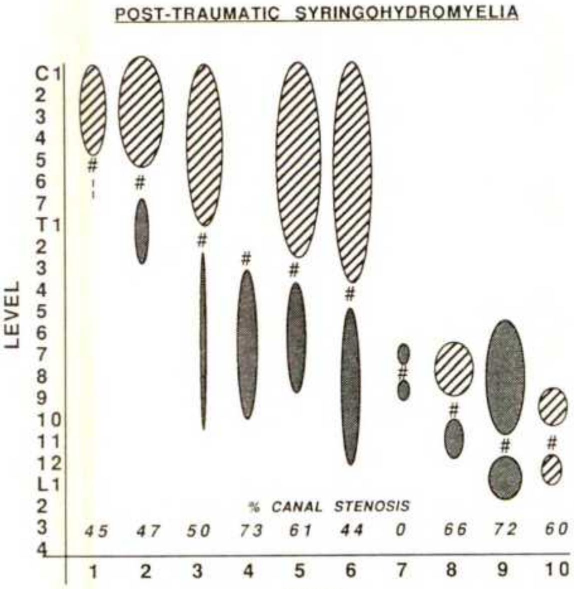


Figure 11. Post-traumatic syringohydromyelia. The vertical extent and maximum transverse diameter of post-traumatic syringes are represented by proportionately-sized ovoids; those with internal septations or fibroglial bands are hatched whilst those with smooth walls are shaded. The level of injury is shown (#) and the percentage canal stenosis is also recorded.

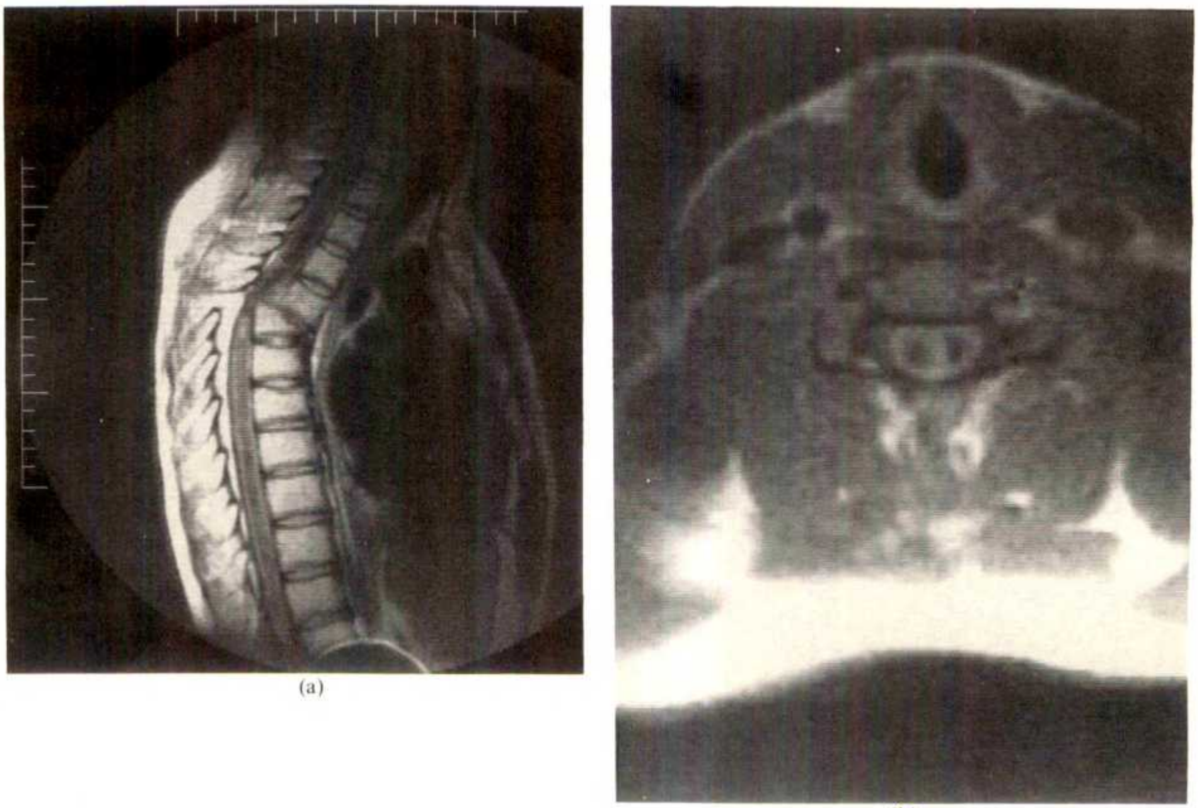
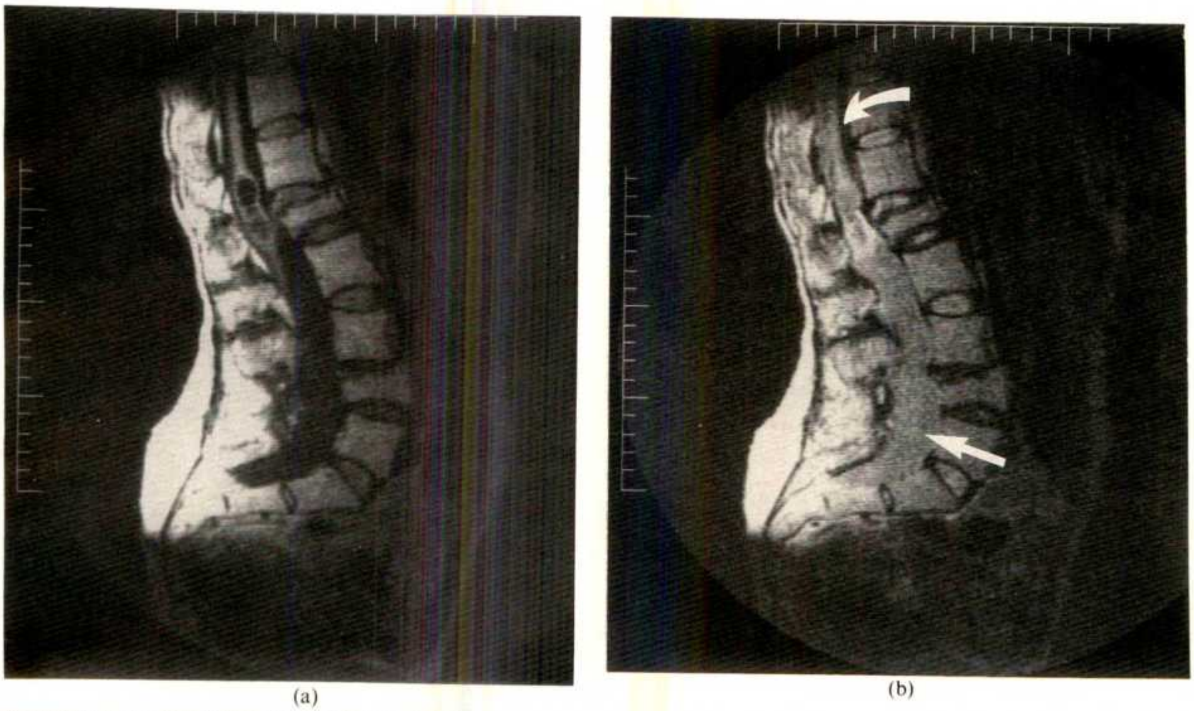

(a) (b)

Figure 12. Sagittal (a) and axial (b) SE 500/40 images 6 months after RTA. Shear type fracture dislocation of C4/5. There is an extensive syrinx (from C1 to T11) which above the fracture is complex with fibroglial bands (b) while, below the fracture level, the syrinx is unilocular. There is marked focal canal stenosis and the enlarged spinal cord completely fills the canal at this level.

advantages compared with CT in being capable of surveying large regions of the spine, in producing direct sagittal images and showing direct evidence of ligament disruption or contusion. The ability to reveal injuries unsuspected clinically and on the basis of conventional radiography is of obvious benefit.

Previous studies have documented the utility of MRI in acute spinal trauma (Kulkarni et al, 1987; Tarr et al, 1987; Beers et al, 1988; Goldberg et al, 1988; Mirvis et al, 1988a; Schaefer et al, 1989). Magnetic resonance imaging is well suited to evaluation of the discovertebral junction and intervertebral discs. In comparison with CT, MRI detects more traumatic disc herniations, epidural haematomas and spinal cord abnormality, though is less sensitive in the detection of posterior element fractures (Tarr et al, 1987). Traumatic cervical disc herniations are probably more common than previously recognized, occurring in 40–50% of cases in some series (Mirvis et al, 1988a; Schaeffer et al, 1989) and in 30% of our material. Acute central injury to the cord (with an intact vertebral column) is more common in the elderly population, in whom the cervical canal is already reduced in size by degenerative disease (Johnston, 1989). Disc herniations in the presence of spondylosis may give rise to an anterior spinal cord syndrome in the absence of vertebral column fractures or dislocations (Mirvis et al, 1988a; Johnston, 1989) and signal changes within the spinal cord may be shown by MRI in such cases (Yamashita et al, 1990).

Vertebral body fractures are readily detected by MRI and CT in most, but not all, cases (Tarr et al, 1987; Mirvis et al, 1988a). In keeping with previous studies of spinal trauma, we found a preponderance of male patients with cervicothoracic and thoracolumbar injuries. In our series, both increased and decreased signal intensity was shown in fractured vertebral bodies, as has been previously reported (Beers et al, 1988). Fractures of the posterior elements were less readily shown (Tarr et al, 1987) but often attention was indirectly drawn to them by the presence of ligamentous abnormalities shown on the STIR sequence. Computed tomography remains valuable in the detection of neural arch fractures in the cervical region and also in demonstration of small bone fragments within the cervical canal which may remain undetected by MRI. In general, osseous lesions are better shown by conventional radiography



(a) (b)

Figure 13. Sagittal SE 500/40 (a) and SE 1600/80 (b) images of a small septated syrinx in conus at level of previous burst fracture. There is moderate focal canal stenosis and the expanded distal cord completely fills the canal at this level. Note the distended distal thecal sac containing CSF of higher signal intensity (arrow) than that above level of block to CSF flow (curved arrow) on T_2WSE and peripheral hyperintensity to syrinx.

and CT, but vertebral alignment may be better appreciated by MRI in the cervicothoracic region (Goldberg et al, 1988). Magnetic resonance imaging is also of value in the diagnosis of multilevel injury and may reveal clinically unsuspected injuries, as was our experience in at least one case. An added advantage is the facility of MRI in demonstrating the cervicothoracic junction region, which, owing to artefacts, may be difficult to demonstrate by conventional radiographs or CT.

There is poor correlation between radiographic appearances of burst fractures (including assessment of posterior element fracture, translocation and degree of canal narrowing) and neurological status, though lumbar burst fractures with more than 50% canal narrowing show an increased risk of instability and neural damage (Willen et al, 1989). The skeletal deformity is well shown by CT, but MRI has the advantage of demonstrating the precise relationships of the spinal cord to the vertebral column or retropulsed fragments at the level of injury (Kulkarni et al, 1987). Magnetic resonance imaging is useful in orientating fragments within the canal, though in severely comminuted burst fractures, CT is capable of showing larger numbers of displaced fragments (Tarr et al, 1987). Where subluxation is present, this is better assessed by MRI than CT; MRI also optimally distinguishes between impingement on the theca or cord by subluxed vertebrae or concurrent haematoma (Tarr et al, 1987).

Coronal (vertical) body clefts in adults are usually the result of either trauma or metabolic bone disease. In traumatic cases, remodelling may result in the late development of a complete vertical cleft into which the cranially and caudally related discs herniate and become apposed, in some cases without desiccation of the central component of the disc (Wilson et al, 1989). Magnetic resonance imaging permits the long term sequelae of disc trauma to be studied non-invasively and is of value in demonstrating which discs become dehydrated or protruded, information which may be of value when surgical fusion is planned.

While ligamentous injuries may be indirectly inferred from conventional radiographic or CT examinations, MRI is uniquely capable of demonstrating ligamentous disruption (Kulkarni et al, 1987; Goldberg et al, 1988; Mirvis et al, 1988a; Beers et al, 1989). We identified disruption of the anterior longitudinal ligament (ALL) in five cases, four of which were thoracolumbar burst fractures. A diagnosis of posterior longitudinal ligament (PLL) rupture was not made in any case. This probably reflects the difficulties encountered in identifying the PLL given the technical limitations of our MRI scanner, rather than the lack of PLL injury. In an autopsy study, Willen et al (1989) found complete or partial rupture of the PLL in all of their patients dying acutely with thoracolumbar burst fractures; avulsion of the ALL from the injured vertebral body and the vertebral body below was seen in 50% of cases and loosening of the ALL in the remainder, but in no case was the ALL completely ruptured. However, in cases treated surgically, an intact PLL is often preserved even though stretched (Webb, Personal communication). The PLL, adjacent cortical bone and CSF are all of low signal intensity on T_1WSE; use of either T_2WSE or gradient-echo techniques to produce high signal intensity CSF should reduce problems of PLL identification. We noted that the PLL was lifted from the underlying vertebral body by either haematoma (presumed) or disc protrusion in five cases; in these, because of the nature of the contained material, the PLL could be clearly identified (though was not ruptured). It is interesting that the PLL in each case appeared to be fixed at the cranial and caudal limits of its elevation at the level of the mid-vertebral body, often at the level of the basivertebral vessels.

Abnormal signal intensity within the interspinous ligaments was often present on both T_1-weighted and T_2-weighted images, but was best appreciated using the STIR sequence, where the high signal intensity of intermuscular fat planes was suppressed. We were unable to differentiate between the changes due to soft tissue contusion, haemorrhage or ligamentous rupture as pathological confirmation was not present in this material. Identification of the true extent of ligamentous injury is important practically and may alert clinicians to the risk of instability and delayed spinal cord compression (Goldberg et al, 1988). Isolated rupture of the posterior ligamentous complex is insufficient to cause instability, though additional rupture of the PLL and posterior annulus fibrosus permits instability in flexion to occur. It was this latter observation which led to the proposal of a three-column spinal structure (Denis, 1984).

In some cases, a line of high signal intensity extending from anteriorly to posteriorly through the injured level can be seen, possibly indicating the regions that have experienced maximal disruptive forces (Beers et al, 1988). This was seen in four of our cases. These findings can, perhaps, be considered as a visual extension of the concept of "fingerprints" of spinal trauma (Daffner et al, 1986), and promise to assist in understanding the mechanisms of vertebral trauma, particularly with regard to ligamentous damage which cannot be shown by other means.

Spinal epidural haematoma may be of variable appearance on CT (Williams & Nelson, 1987) and is frequently difficult to detect in acute cervicothoracic injury as a result of beam hardening artefacts in the shoulder region. While the MRI appearances of epidural haematoma are relatively characteristic (Rothfus et al, 1987; Bernsen et al, 1988; Pan et al, 1988) there may also be contributions to epidural thickening from venous engorgement and oedema (Beers et al, 1988), all of which result in increased signal intensity on T_2-weighted images. Use of the STIR sequence facilitates the diagnosis of thoracic region epidural haematoma, where suppression of the signal from normally situated posterior epidural fat leads to greater conspicuity of epidural haematoma. In contrast to parenchymal haemorrhage, extraparenchymal blood appears of high signal intensity on short TE images and may be isointense on long TE images. In experimental animal models, this is probably because of the rapid formation of methaemoglobin where the wounds are exposed to atmospheric oxygen (Hackney et al, 1986). Traumatic spinal epidural haematoma has previously been considered to be uncommon (Pan et al, 1988), but in our material was shown in 41% of examinations performed within 7 days. Two of our recent cases, imaged within a few hours of injury and with incomplete neurological deficits, were operated on following the MRI demonstration of extensive epidural haematoma causing cord compression. The MR images were of value in planning the surgical approach and extent of exploration, as has been suggested by other workers (Beers et al, 1988). The role of such early operative intervention has yet to be fully evaluated. Other workers have described extradural haematoma arising distant to the fracture site, but this was not seen in our material (Goldberg et al, 1988).

Spinal cord

Clinical evaluation of spinal trauma cannot reliably distinguish between cord transection, necrosis, haemorrhage or oedema, as shown by those patients who improve after initially complete clinical lesions. Electrophysiological testing is of limited prognostic value as only specific pathways are evaluated (Hackney et al, 1986). Assessment is further complicated by the fact that the clinical level of spinal cord abnormalities may be different from the site of injury.

The late sequelae of spinal trauma include spinal cord atrophy, tethering, myelomalacia and syringohydromyelia. These may be localized at the injury site or extend extensively into non-traumatized regions of the cord. Abnormalities of the vertebral column and intervertebral discs may occur due to the original injury or as a result of mechanical instability subsequent to previous decompressive surgery and these may, in turn, contribute to further cord injury (MacDonald et al, 1988). Magnetic resonance imaging readily demonstrates the relationship of the thecal sac and spinal cord to the vertebral column and provides a non-invasive means of demonstrating spinal cord displacement or compression and the presence of cord atrophy, tethering, myelomalacia or syringohydromyelia.

Computed tomography scanning and CT myelography are insensitive to spinal cord abnormalities following trauma (Quencer et al, 1986; Tarr et al, 1987; Beers et al, 1988; Goldberg et al, 1988). Magnetic resonance imaging provides a wealth of information, though pathological correlation has frequently not been obtained. *In vitro* micro-imaging studies in animal models have shown loss of the grey/white matter interface at the level of injury and low signal intensity regions representing haemorrhage (Lemaire et al, 1990). Other authors have described very low signal intensity lesions on long TE sequences with iso- or hypointensity on short TE sequences corresponding to pathologically confirmed cord haemorrhage and the presence of deoxyhaemoglobin. More diffuse high signal intensity changes in the cord seen on long SE sequences correspond to oedema, but differentiation of necrosis from non-necrotic oedema is not possible (Hackney et al, 1986).

In human studies, MRI has demonstrated various patterns of abnormality within the acutely injured spinal cord. Although pathological material is sparse, reasonable correlation of MRI patterns with pathology has been obtained (MacDonald et al, 1988). Spinal cord swelling is best shown on T_1-weighted images (Beers et al, 1988). Focally increased signal intensity on T_2WSE probably represents oedema while focal hypointensity on long TE images is consistent with the presence of deoxyhaemoglobin (Beers et al, 1988). At high field strength (1.5T), Kulkarni et al (1987) describe three patterns of cord damage in acutely spine injured patients corresponding to (1) central haemorrhage which increased with time, (2) central petaechial haemorrhage resolving with time and (3) oedema and contusion only. Prognosis seems to relate to these categories, being worst in those with intraparenchymal haemorrhage (Pattern 1) (Kulkarni et al, 1987; Schaefer et al, 1989; Bondurant et al, 1990) while those with oedema or petaechial haemorrhages exhibit the potential for some neurological recovery (Kulkarni et al, 1987; Schaefer et al, 1989; Bondurant et al, 1990). Type 2 changes were the commonest (63%) and were usually associated with clinical improvement (Kulkarni et al, 1987). Patients in both Patterns 1 and 2 were seen without neurological deficit. We observed the Type 2 pattern in all but one of our cases. Focal cord contusions encompassing only one spinal segment or less are associated with less severe neurological deficits than more extensive contusions (Schaefer et al, 1989). In the case of spinal cord haemorrhages, peripheral hyperintensity around central hypointensity may be seen on follow-up at 3–7 days in cases where initial scanning showed just hypointensity (Kulkarni et al, 1987; Quencer, 1988). This was the pattern seen in one of our cases imaged at 7 days after injury (see Fig. 5). In our experience, cord contusion was only rarely an isolated abnormality, evidence of skeletal injury frequently being present. Patients with a central cord syndrome typically have no discernible skeletal injury (Johnston, 1989; Yamashita et al, 1990).

The changes seen on sequential MRI appear to be of prognostic significance. Five MRI patterns have been described in patients scanned sequentially following injury (Yamashita et al, 1990). Those patients showing Type I (normal signal intensity on both T_1WSE and T_2WSE) in the acute stage frequently showed no progression of MRI appearances and had a good neurological outcome. Of those with Type II changes (normal T_1WSE, high signal T_2WSE) in the acute stage, the subgroup showing resolution to Type I had an improved neurological outcome while those with persisting Type II changes showed no improvement. Persisting cord compression was observed in 83% of those with Type II pattern and if this was relieved, neurological outcome was improved in some cases. Patients with a central cord syndrome showed Type II changes in two thirds of the cases, often without associated vertebral column injury. Some of these progressed to gliosis only, while others showed progressive liquefactive necrosis. Type IV changes (atrophy) were only seen as a late phenomenon in their patients, all of whom had a long history of post-traumatic myelopathy or cord compression. We have observed atrophy in patients examined as early as 4 months after injury, although in the majority of cases atrophy was only seen in those scans obtained 2 years or more following trauma. Patients developing Type III changes (low T_1WSE, high T_2WSE) suggesting myelomalacia had a poor neurological outcome, as did those with Patterns IV and V (atrophy and syrinx).

Clinico-pathological studies have resulted in the concept of a spectrum of post-traumatic spinal cord pathology from arachnoiditis to microcystic degeneration to syringohydromyelia (MacDonald et al, 1988; Stevens et al, 1988; Yamashita et al, 1990). Ascending and descending post-traumatic myelopathy is thought to begin at the time of injury or soon after and may involve mechanisms such as the release of destructive enzymes, free radical products or other toxic agents (Stevens et al, 1988; Fox et al, 1988). Central or dorsicentral cores of necrotic tissue may extend for several segments from the level of injury and these could liquefy and form a cavity. Conversion of this area of necrosis into a true cyst may take months to years and this probably accounts for the apparent continuum of non-cystic to cystic myelopathy to syrinx. The rate of progression in individual cases appears to be highly variable. Our study included patients examined at 6 months after injury and in whom examples of myelomalacia, atrophy and syringohydromyelia were all seen. We found no significant difference in the interval between trauma and MRI in those patients with myelomalacia (mean, 9.5 years) compared with those with atrophy (mean, 10.1 years).

Delayed CT following water-soluble myelography may show contrast accumulation within the spinal cord in both cystic and non-cystic myelopathy (Stevens et al, 1988), but MRI appears to be more reliable in predicting the presence of surgically-drainable syringohydromyelia (Quencer et al, 1986; Quencer, 1988). However, microcystic degeneration may mimic these appearances, particularly when lesions are small (MacDonald et al, 1988). Intra-operative ultrasound should permit an accurate distinction to be made before myelotomy is undertaken (MacDonald et al, 1988; Quencer, 1988).

Syringohydromyelia may occur as a consequence of extramedullary compressive lesions, possibly owing to ischaemia of the cord with secondary degeneration of the grey matter or by filling of the central canal by extrachoroidally produced CSF (Castillo et al, 1988). Extrinsic compression may lead to neuroglial damage with enlargement of extracellular perivascular spaces;

the formation of arachnoid adhesions may alter CSF dynamics so that abnormal entry of CSF into the cord via the enlarged Virchow–Robin spaces results in syringohydromyelia (Castillo et al, 1988) which enlarges and propagates due to a water-hammer effect (Sherman et al, 1986). We observed differing patterns of syrinx above and below the level of injury in all cases of cervicothoracic fracture dislocation, each associated with significant focal canal stenosis. In these cases, the spinal cord was noted to fill the narrowed spinal canal completely. If there is a high degree of subarachnoid block and focal compression of the syrinx by a fracture/dislocation, locally altered CSF dynamics may result in turbulence of CSF within the syrinx above the block and stagnation below, resulting in a variable appearance of the syrinx in these two locations (Quencer, 1988). This was found in four out of six cervicothoracic and one of four thoracolumbar injuries where a syrinx had developed. The moderate to severe canal stenosis that we have observed and the associated differing patterns of syrinx above and below may also reflect the severity and mechanism of the original injury, possibly modified by abnormal spinal motility relating to the injury and/or subsequent surgical intervention.

In some cases, trauma may result in the formation of rents in the spinal cord (perhaps due to laceration by bone fragments) which communicate directly with the spinal subarachnoid space and result in the formation of syringes which are clinically indistinguishable from those formed more conventionally. Fissures in the spinal cord communicating with the spinal subarachnoid space have also been shown in syringomyelia associated with Chiari malformations (Aubin et al, 1987). These fissures may enlarge as a result of a ball-valve effect due to adhesions and may be improved by shunting. Post myelographic CT may demonstrate immediate entry of contrast into the cord and high resolution MRI is also capable of demonstrating these fissures (Post et al, 1987; Stevens et al, 1988), though none was identified in our material.

Demonstration of the complex nature of syringohydromyelic cavities requires use of both sagittal and axial imaging planes (Aubin et al, 1987). Partial septations or fibroglial remnants are commonly observed, particularly above the level of injury, and their demonstration may be important if surgical drainage is contemplated, since they may indicate the need for multiple drains or syringotomies. When T_2WSE are used, the contents of some syringes (particularly when large) are of lower signal intensity than CSF, probably indicating the presence of pulsatile fluid shifts leading to reduced signal intensity due to both time of flight and phase shift phenomena (Sherman et al, 1986). This has been described in syringes of Chiari associated (Sherman et al, 1986; Aubin et al, 1987), tumour-associated (Sherman et al, 1987) and post-traumatic origin (Sherman et al, 1986; Quencer, 1988). Those cysts demonstrating low signal intensity on non-gated T_2-weighted sequences may be undergoing active expansion and a stronger case for surgical shunting of these syringes may be made (Quencer, 1988). In our series, T_2WSE images were obtained in only one case with a syrinx; this demonstrated a central flow void within the syrinx as well as peripheral hyperintensity around the syrinx.

Areas of high signal intensity on T_2-weighted images surrounding syringes have been noted and are due to surrounding gliosis, oedema, microcystic change or demyelination (Sherman et al, 1986). Gliosis occurs in response to distending forces acting upon the syrinx walls and is therefore seen predominantly at the circumference of the syrinx and also at its cranial apex where it develops to withstand the upward pulsations of the syrinx fluid (Sherman et al, 1986). In patients with extrinsic cord compression due to spondylosis, Jinkins et al (1986) have described features consistent with central grey matter necrosis and cavitation occurring at the level of compression, possibly due to repeated trauma or ischaemic change. In some cases, thin central regions of necrosis or cavitation extending both cranially and caudally to the compressive level were observed. The factors responsible for the initial formation and later propagation of these abnormalities are probably different (Sherman et al, 1986; Stevens et al, 1988), but may be important where continuing spinal cord compression is present as a result of post-traumatic canal stenosis.

Post-traumatic syringomyelia may be limited to a single spinal level at the site of injury or involve the entire cord (Aubin et al, 1987). Distinguishing between a small syrinx or an area of myelomalacia may be difficult using MRI: syringes usually demonstrate a sharp interface with the adjacent cord, contain no internal signals and may show a flow void. Myelomalacia usually involves only a short segment of the cord, is limited to the site of injury and has a less distinct interface with the surrounding cord and has no flow void (Quencer, 1988). This judgement is of only academic interest if the syrinx is very small (less than 1 cm) as this would not be surgically drained. Intra-operative ultrasound is capable of distinguishing between these two entities, but requires surgical exposure of the theca.

Conclusion

The contribution of MRI to the overall management of acutely and chronically spinal injured patients has yet to be fully defined. In the acute phase, the greatest potential role is in the identification of remediable intraspinal problems in those patients with an incomplete neurological deficit. The soft-tissue components of spinal trauma are particularly well demonstrated with MRI and the incidence of disc herniation and epidural haematoma is far greater than previously suspected. The precise level of intramedullary abnormalities may be shown though differentiation between oedema, haemorrhage, gliosis or microcystic myelopathy remains suboptimal (Fox et al, 1988). The signal patterns appear to be of prognostic importance (Yamashita et al, 1990).

In the more chronic stages, surgically treatable problems may be assessed non-invasively and without hazard to the patient. Syringomyelia is readily identified, although intra-operative ultrasound may be required to distinguish microcystic myelomalacia from smaller syringes. Continuing cord compression is clearly shown and may be clearly distinguished from established cord atrophy.

Apart from conventional radiography, MRI is recommended as the investigation of choice in spinal injury, particularly when a neurological deficit is present or is progressing.

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Pitfalls of bone scintigraphy in suspected hip fractures

By *S. L. Lewis, MA, FRCS, J. I. S. Rees, BSc, FRCR, G. V. Thomas, FRCR and L. A. Williams, FRCR, FRCS

Departments of Radiology and *Orthopaedic Surgery, Cardiff Royal Infirmary, Cardiff

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Abstract. In a review of 2617 patients who were admitted with a suspected fractured neck of femur over a period of five years, 213 had normal or equivocal plain radiographs, and were subsequently investigated by bone scintigraphy. Normal scans were obtained in 127 (60%) cases. Of the remaining 86 cases, 82 (38%) were reported to show fractures of the proximal femur, three showed pubic ramus fractures, and one acetabular fracture was demonstrated. Review and follow-up has revealed eight false positive and two false negative scans. The various factors accounting for these errors are considered, and the clinical implications discussed. Careful analysis of accompanying plain radiographs is stressed when interpreting scintigrams.

A common problem in orthopaedic trauma units is that of the elderly patient who presents with an acutely painful hip after a fall and normal plain radiographs. A proportion of these patients who have persistent pain and reluctance to weight bear will subsequently be shown to have femoral neck fractures, but this may not become apparent by conventional radiography until displacement has occurred, with resulting increased risk of non-union and avascular necrosis (Garden, 1964).

Bone scintigraphy has been advocated as a highly sensitive and specific method of detecting these occult fractures at an early stage (Holder et al, 1990). A previous study performed at this centre on a series of 43 elderly patients with suspected hip fractures and normal plain radiographs, who all underwent bone scans, showed bone scintigraphy to be highly reliable in the identification of these fractures, with no false positive or false negative results (Fairclough et al, 1987). The aim of our study was to assess, retrospectively, the value and limitations of bone scintigraphy in suspected hip fracture by reviewing our experience over the past five years.

Patients and methods

The study group consisted of 2617 patients admitted to the Cardiff Royal Infirmary over a period of over 5 years, from March 1983 to October 1988, with a clinically suspected fracture of the femoral neck. Standard anteroposterior (AP) and lateral radiographs were obtained in all cases. Radionuclide bone scans were performed in 213 patients where the plain radiographs were reported to be either normal or equivocal and there was enough clinical suspicion of a fracture.

The average age of the patients who underwent scintigraphy was 81 years (range 51–98) with a female to male ratio of 4 : 1. Anterior images were obtained two hours following the injection of 500 MBq of ^{99}Tc^{m}-methylene disphosphonate, using an IGE 400T gamma camera with a high resolution, low energy, parallel hole collimator. When indicated a pin-hole collimator was used to obtain localized anterior views. Bladder catheterization was occasionally necessary to improve visualization of the pelvis and hips, but was not routinely carried out.

Most scans were performed within 2 to 5 days of injury, although a few studies were performed later than this. No scans were obtained sooner than 48 hours after injury. The films and scintigrams were reviewed at least 6 months following admission and the final diagnoses were based on the subsequent clinical progress, radiographic follow-up and findings at operation for those who underwent surgery.

Results

Typical scintigraphic appearances of radiographically "occult" subcapital and intertrochanteric fractures are shown in Figs 1 and 2, respectively.

The vast majority of the 2617 patients who presented with an acutely painful hip and a clinically suspected fracture had initial radiographs which confirmed the diagnosis and were treated appropriately. Of the 213 scintigraphic examinations, 127 (60%) were reported to show no evidence of a fracture.

There were two false negative studies, both of which were reported to show avascular femoral heads but no evidence of a femoral neck fracture. The first of these was a 73-year-old woman who presented with a painful left hip after a fall. Initial plain radiographs were normal, and a bone scan (Fig. 3a) performed 7 days following injury showed poor uptake of isotope in the left femoral head, but no localized increased activity to suggest a fracture. A repeat film the following day, however (Fig. 3b), revealed a displaced subcapital fracture.

The second false negative study was of a 95-year-old woman who also had normal initial plain radiographs. A bone scan (Fig. 4a) performed 4 days after injury, again showed an avascular right femoral head but no femoral neck fracture. However, the clinical signs of femoral neck fracture were such that internal fixation with two Hansson pins was performed. The patient's symptoms were relieved, and she was able to walk.

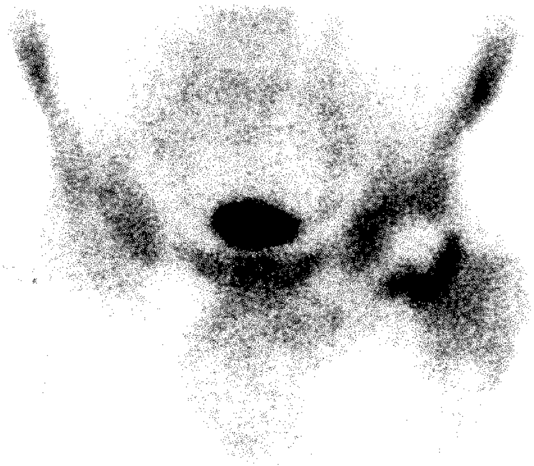


Figure 1. Subcapital fracture in a 72-year-old woman 4 days following injury. Anterior image shows linear uptake in the left femoral neck, and an avascular femoral head. Plain radiographs were normal.

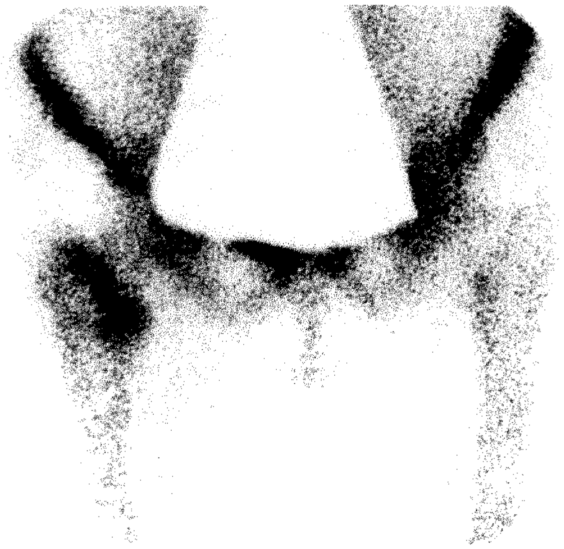
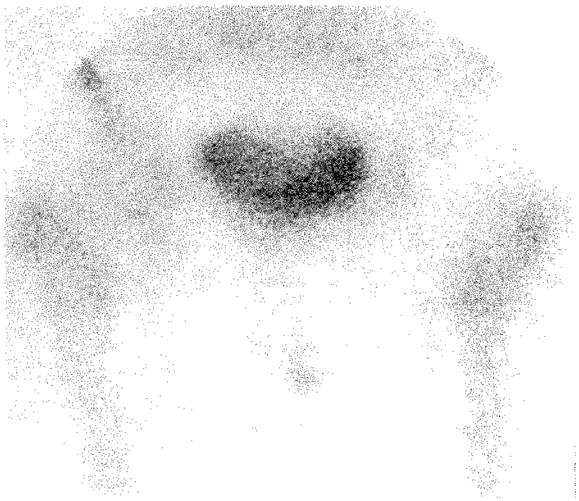


Figure 2. Intertrochanteric fracture in a 76-year-old woman. Anterior image, showing increased activity along the whole length of the intertrochanteric region. Plain radiographs were normal.

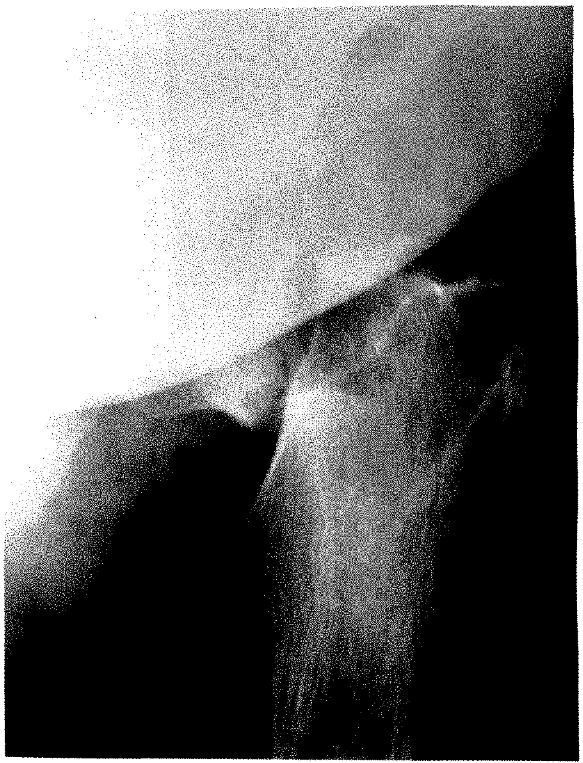
Post-operative radiographs revealed a subcapital fracture, and a bone scan 2 months later (Fig. 4b) showed increased uptake across the fracture site and also some uptake within the femoral head indicating early revascularization.

All remaining patients with negative scintigrams were mobilized without complication and none developed femoral neck fractures.

Of the 86 scintigrams showing fractures, 71 were



(a)



(b)

Figure 3. False negative study in a 73-year-old woman. (a) Anterior view of a bone scan performed 7 days after injury showing a "cold" left femoral head but no fracture. (b) Anteroposterior radiograph 24 hours later, showing an obvious displaced subcapital fracture.

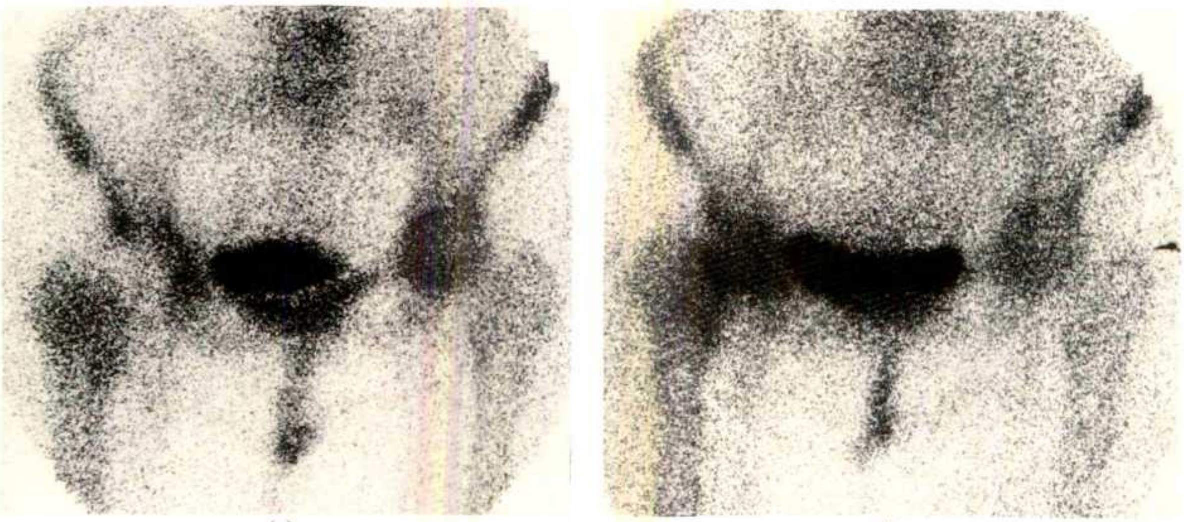
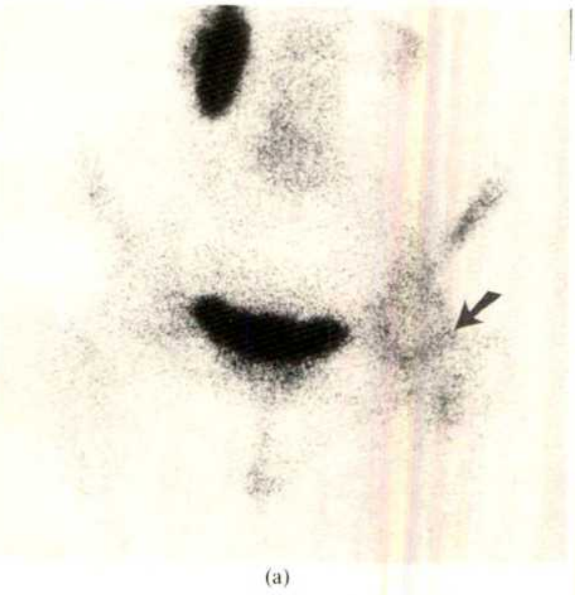


Figure 4. False negative bone scan. Anterior views in a 95-year-old woman. (a) Four days following injury, showing a "cold" right femoral head but no femoral neck fracture. (b) Repeat bone scan 2 months post-operatively. The subcapital fracture is demonstrated, and there is now some uptake within the femoral head indicating revascularization.

reported to show fractures of the proximal femur which were internally fixed. In addition, fractures of the greater trochanter (11), pubic ramus (three) and acetabulum (one) were demonstrated and this group of patients was treated conservatively. Review of the above cases, however, demonstrated eight false positive studies.

One patient, a 96-year-old woman, was diagnosed as


(a)

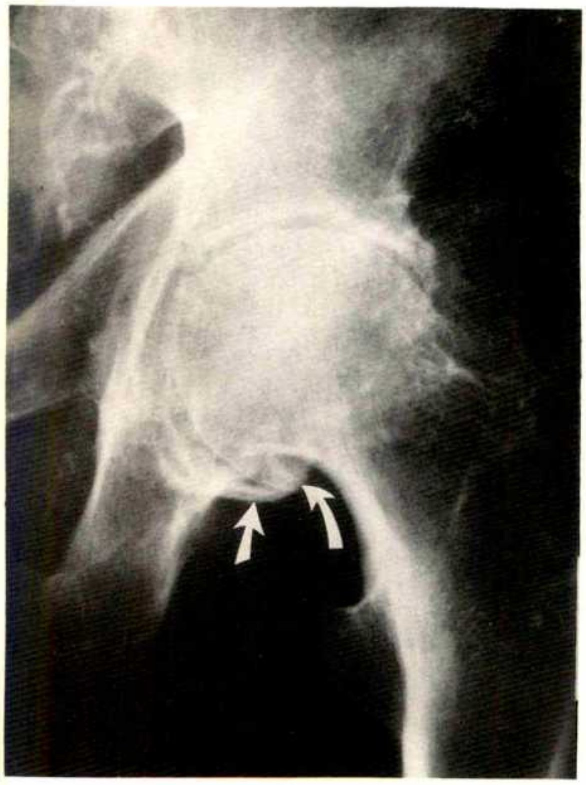

(b)

Figure 5. False positive study in a 96-year-old woman. (a) Anterior view of a bone scan showing faint linear uptake of isotope across the left femoral neck (arrow) simulating a femoral neck fracture. (b) Anteroposterior radiograph same day as bone scan showing rim osteophytes around the femoral head (curved arrow) and a low acetabular roof (straight arrow).

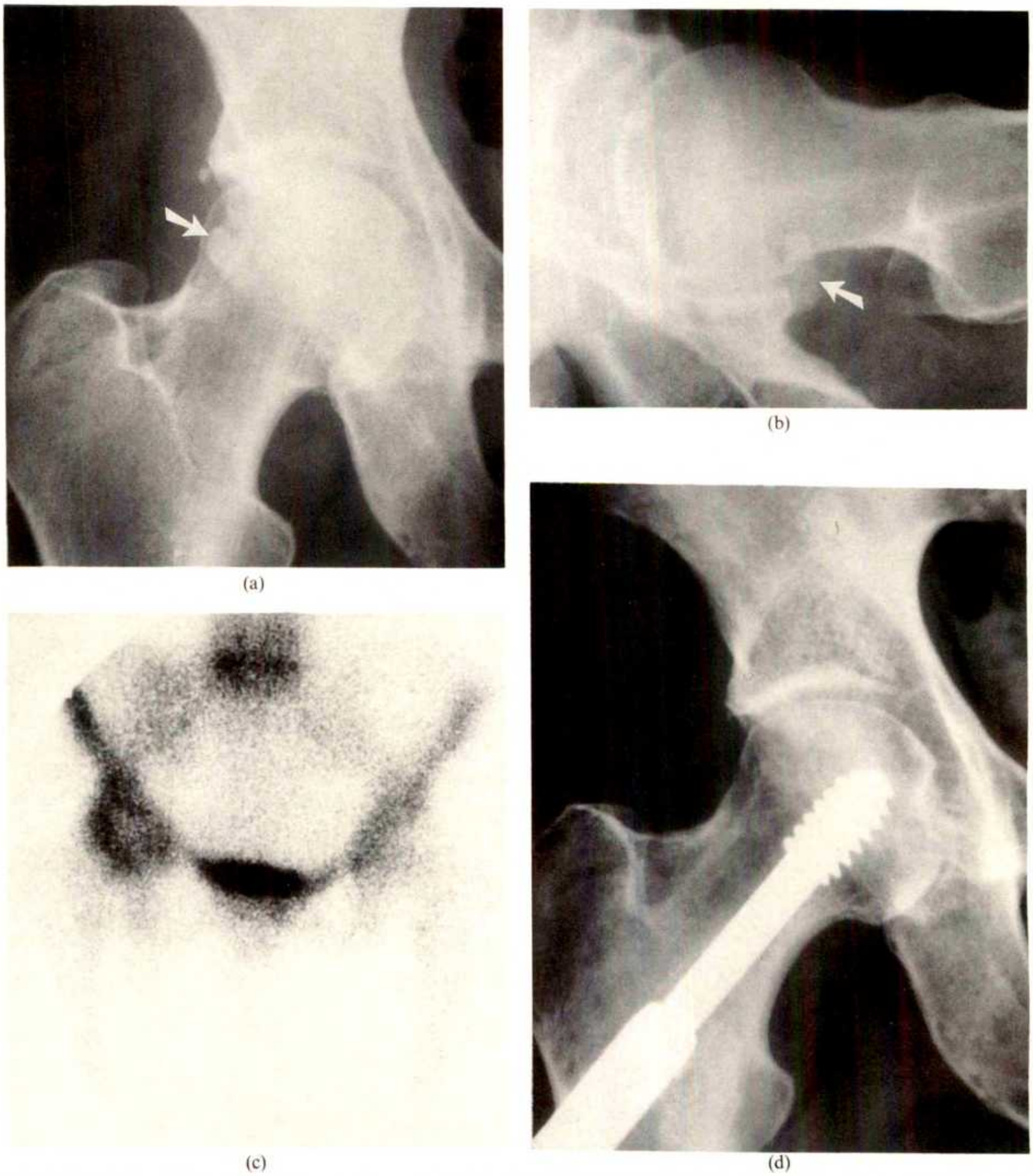


Figure 6. False positive study in a 53-year-old woman. (a) and (b) AP and lateral radiographs showing an area of calcification (arrow) related to the posterior capsule of the right hip. (c) Bone scan, anterior image, showing increased activity in the region of the right femoral neck simulating a fracture. (d) Repeat AP radiograph 4 months post-operatively. The calcified area has disappeared. No evidence of a healed fracture of the femoral neck.

having a subcapital fracture on the basis of a faint linear area of uptake across the left femoral neck (Fig. 5a). As a result the hip was internally fixed with Hansson pins, but follow-up films up to 30 months post-operatively have consistently failed to show any evidence of a healing fracture. Review of the plain radiographs, however, shows advanced degenerative changes at the hip, resulting in a low acetabular roof and rim osteophytes around the femoral head (Fig. 5b). Circumferential uptake of isotope in this region would

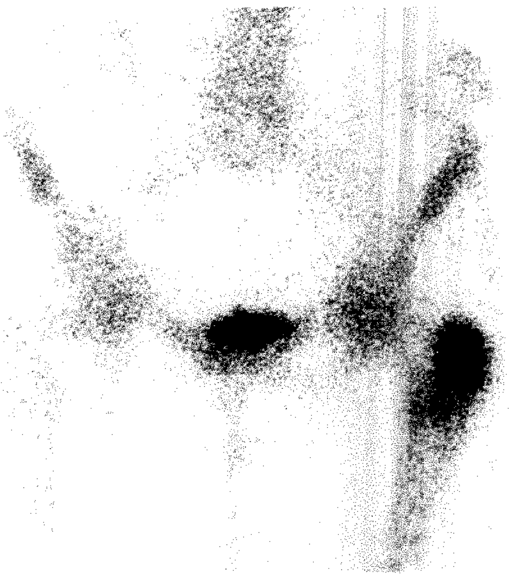


Figure 7. False positive study. Bone scan, anterior view, showing marked activity localized to the left greater trochanter. There is also some diffuse activity elsewhere in the proximal femur related to disuse. Plain radiographs were normal. Final diagnosis: trochanteric bursitis.

explain the linear band of activity overlying the femoral neck, simulating a femoral neck fracture.

A second false positive study was unveiled in a 53-year-old woman who presented with a 2-day history of right hip pain. She could not recall a recent injury to the hip, but remembered falling down a flight of stairs 2 months earlier. Plain radiographs (Fig. 6a and 6b) showed an area of calcification related to the posterior capsule of the right hip, but no fracture. A subsequent bone scan (Fig. 6c) was reported as highly suggestive of a fracture and the hip was internally fixed. However, a film 4 months post-operatively (Fig. 6d) showed the calcified area had disappeared, and there was still no evidence of a healing fracture. A follow-up bone scan at 21 months was also normal. We believe the diagnosis here was an acute calcific capsulitis of the hip.

Finally, there was a group of six patients all having similar appearances on bone scintigraphy, who we believe were falsely diagnosed as greater trochanteric fractures. The scans showed increased uptake of isotope localized to the greater trochanter (Fig. 7). The scintigrams alone were indistinguishable from those in patients with greater trochanteric fractures, but the initial plain radiographs in the above group were normal and follow-up radiographs remained normal. In each case, the patients' symptoms gradually resolved on conservative treatment, and the patients were fully mobilized. We believe the diagnosis in these six patients was trochanteric bursitis.

Discussion

The early detection of occult fractures of the hip has important therapeutic, economic and medico-legal implications and bone scintigraphy has clearly been shown in this study and in previous studies, to be of great value (Holder et al, 1990; Slavin et al, 1986). Prompt surgical treatment results in an improved prognosis, allows earlier mobilization and reduces hospitalization with its attendant risks of complications such as pneumonia and pulmonary emboli.

Contrary to a previous study from our centre, this retrospective study has questioned the total reliability of bone scintigraphy in identifying occult fractures of the hip and has highlighted several false positive and two false negative examinations.

One false positive study was related to degenerative disease of the hip joint. As a "rule of thumb", subcapital fractures very rarely occur in association with osteoarthritis of the hip joint, whereas intertrochanteric fractures are far more common (Colhoun et al, 1987). This may be due to the thickening and buttressing of the femoral neck that occurs with degenerative change. Therefore, the increased uptake of isotope in the acetabulum, femoral head and femoral neck that occurs in association with osteoarthritis is not usually a problem in masking subcapital fractures. However, care must be taken when interpreting these scintigrams, as a low acetabular roof or rim osteophytes surrounding the femoral head may give rise to a linear band of activity overlying the femoral neck, simulating a fracture (Fig. 5a).

The uptake of radionuclides in soft tissue calcification is well recognized (Galasko & Weber, 1984) and accounts for the false positive diagnosis of a fracture in the 53-year-old woman whose final diagnosis was acute calcific capsulitis of the hip. When plain radiographs reveal periarticular calcification, the possibility of extraosseous radionuclide uptake must always be considered.

The patients who showed increased isotope activity localized to the greater trochanter can be a difficult group to diagnose. In many cases, a close inspection of the initial or repeat plain radiographs will reveal a greater trochanteric fracture. We believe that the six cases we identified with normal plain radiographs who subsequently showed symptomatic improvement on conservative treatment are typical of trochanteric bursitis. Management, however, will be unaffected whether the diagnosis is of a greater trochanteric fracture or bursitis, as both groups of patients are treated conservatively by early mobilization.

Bone scintigraphy will also demonstrate fractures of the surrounding skeleton, for example of the pubic rami and acetabulum, not only explaining the cause of the pain but also allowing early mobilization.

The two false negative scans occurred in two elderly women aged 73 years and 95 years. Both had similar scintigraphic appearances, showing avascular femoral heads, but no localized activity to suggest a fracture. Both were subsequently shown to have femoral neck fractures. The reason for the lack of uptake at the fracture site is not clearly understood. It has been suggested that in older osteoporotic patients, significant focal accumulation of activity may not occur until 72 hours after injury (Matin, 1979), but our two cases were imaged at 7 days and 4 days following injury, by which time some focal activity at a fracture site would be expected. In retrospect, a cold femoral head combined with a recent history of a fall in an elderly patient should have been interpreted as highly suggestive of a fracture, despite the absence of the typically increased uptake at the fracture site.

To conclude, we believe that bone scintigraphy remains a very useful test for detecting occult fractures of the hip and surrounding skeleton, provided careful interpretation is made within the context of the clinical findings and plain radiographs, to avoid the diagnostic pitfalls of this investigation.

Acknowledgments

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Measurement of tissue perfusion by dynamic computed tomography

By K. A. Miles, MB, BS, FRCR

Departments of Radiology and Nuclear Medicine, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, UK

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Keywords: Dynamic, Computed tomography, Perfusion, Measurement

Abstract. A method for quantifying tissue perfusion by dynamic computed tomography (CT) is described. By applying a nuclear medicine data processing technique to time-density data from a single-location dynamic CT sequence, tissue perfusion can be determined from the maximum gradient of the tissue time–density curve divided by the peak enhancement of the aorta. Using this method, splenic perfusion was measured at 1.2 ml min^{-1} ml^{-1}, normal renal cortical perfusion at 2.5 ml min^{-1} ml^{-1} and normal renal medullary perfusion at 1.1 ml min^{-1} ml^{-1}. Changes in cortical and medullary perfusion in renal failure and hypertension were demonstrated. The ability of dynamic CT to provide quantitative functional information is not well recognized and is potentially of value when studying structures, such as the renal cortex and medulla, that cannot be anatomically resolved by standard functional imaging techniques.

Dynamic computed tomography (CT) describes a rapid sequence of images acquired after the injection of intravascular contrast medium. If the sequence of scans is performed at the same slice location it is possible to construct time–density curves (TDCs) by defining a region of interest (ROI) over a particular structure. The curve will display the change in X-ray attenuation, and hence the change in iodine concentration within that structure with time. In this way, it is possible to treat the contrast agent as a physiological indicator and gain information about function.

The aim of this study was to determine whether quantitative information about tissue perfusion could be obtained from dynamic CT by applying a nuclear medicine data processing technique to the time–density data.

Patients and methods

The nuclear medicine data processing technique used was developed by Peters et al (1987a) to allow measurement of blood flow from first-pass studies using radioisotopes not completely extracted by the organ studied. The method was subsequently validated in animals (Peters et al, 1987b) and is based on the determination of blood flow as a proportion of cardiac output using radiolabelled microspheres. A time–activity curve over an organ after the injection of microspheres into the left ventricle will rise and reach a maximum height H (cts s^{-1}).

$$\frac{\mathrm{OBF}}{\mathrm{CO}} = \frac{H \times a}{\text{Dose injected}} \tag{1}$$

where OBF is organ blood flow and CO is cardiac output. (The dose injected will be measured in MBq and a is a correction factor relating cts s^{-1} to MBq determined by detector efficiency and photon attenuation). If one considers the integrated arterial time–activity curve corrected for recirculation using a gamma function fit, its shape will be the same as that obtained from the organ using microspheres but reaching the plateau at a value A (cts) and with a maximal slope g_{arterial} (cts s^{-1}). A is also the area under the arterial curve before integration and g_{arterial} will be its maximum height. The integrated arterial curve and the organ curve will be related as follows:

$$\frac{g_{\text{organ}}\ (\text{cts s}^{-2})}{g_{\text{arterial}}\ (\text{cts s}^{-1})} = \frac{H\ (\text{cts s}^{-1})}{A\ (\text{cts})} \tag{2}$$

where g_{organ} is the maximal slope of the organ time–activity curve (cts s^{-2}). However, a tracer that is not completely extracted by the organ on its first pass, such as ^{99}Tc^{m}-DTPA, will produce a time–activity curve that will not reach this plateau value, but its maximal slope, g_{organ} will be the same as that obtained using microspheres. Thus by using Equation (2) to substitute for H in Equation (1):

$$\frac{\mathrm{OBF}}{\mathrm{CO}} = \frac{A}{\text{Dose injected}} \times \frac{g_{\text{organ}}}{g_{\text{arterial}}} \times a. \tag{3}$$

Intravascular contrast medium has pharmacokinetics very similar to those of DTPA and thus the technique can be applied to dynamic CT by constructing TDCs from the aorta and the tissue to be studied. The concentration of contrast medium within any ROI can be determined with an increase in attenuation of 25 HU indicating an iodine concentration of 1 mg ml^{-1} (Hindmarsh, 1975). The correction factor a is not required with CT as A is measured in HU s and the dose injected can be expressed in HU ml. (As an iodine concentration of 1 mg ml^{-1} is equivalent to 25 HU, 1 mg of iodine is equivalent to 25 HU ml.) As it is concentration, *i.e.* the amount of iodine per ml of tissue, that is measured, rather than total organ iodine, it is blood flow per ml of tissue, or perfusion, that is determined. Thus for CT:

$$\frac{\text{organ blood flow/ml tissue}}{\text{cardiac output}} = \frac{A\ (\text{HU s})}{\text{Dose (HU ml)}} \times \frac{g_{\text{organ}}\ (\text{HU s}^{-1})}{g_{\text{arterial}}\ (\text{HU})} \qquad (4)$$

Furthermore, as the cardiac output can be determined by dynamic CT from the injected dose of iodine and the area under the arterial TDC after correction for recirculation (A) (Axel et al, 1979) by:

$$\text{CO} = \frac{\text{Dose injected (HU ml)}}{A\ (\text{HU s})} \qquad (5)$$

the tissue perfusion is thus given by:

$$\text{tissue perfusion (ml s}^{-1}\text{ ml}^{-1}\text{ tissue)} = \frac{g_{\text{organ}}\ (\text{HU s}^{-1})}{g_{\text{arterial}}\ (\text{HU})} \qquad (6)$$

g_{organ} is derived from the maximum gradient of tissue TDC and g_{arterial} is given by the peak height of the arterial TDC (before integration and after subtraction of the pre-contrast medium attenuation value). A multiplication factor of 60 converts ml s^{-1} ml^{-1} to ml min^{-1} ml^{-1}. The advantages of applying this method to CT are its simplicity and the avoidance of the correction factors required when using radioisotopes.

The patients studied were those undergoing dynamic CT for staging of renal carcinoma, diagnosis of renal vein thrombosis in the nephrotic syndrome or diagnosis of renal artery stenosis. The CT machine used was an IGE 8800 and a single-location dynamic sequence was performed at the level of the renal veins with scans performed as rapidly as possible, *i.e.* every 6 seconds, during quiet breathing. Fifty millilitres of iopamidol (370 mg ml^{-1}) were injected intravenously by hand as rapidly as possible and TDCs were derived from ROIs constructed over the abdominal aorta and the organ to be studied. Regions of interest were made as large as possible to reduce the effects of photon noise whilst avoiding partial volume effects.

To validate the method, TDCs derived from 12 spleens were studied and the value for splenic perfusion determined was compared with values derived for humans using intra-arterial xenon (Williams et al, 1968). The kidneys studied were contralateral kidneys in patients with renal tumours (18 kidneys), apparently normal portions of kidneys containing renal tumours (nine kidneys), patients with known renal failure (four kidneys) and hypertensive patients treated with captopril (six kidneys) and without (two kidneys). TDCs were constructed from the renal cortex and medulla.

Results

The mean value of splenic perfusion determined by CT was 1.2 ml min^{-1} ml^{-1} with a standard deviation of 0.4 ml min^{-1} ml^{-1}. The mean values and standard deviations for the renal cortex and medulla in the groups of kidneys studied are displayed in Figs 1–4 and examples of time–density curves are given in Fig. 5.

There was no significant difference in cortical or medullary perfusion in the kidneys containing tumour when compared with normals, and perfusion appeared normal even in one case where the renal vein was occluded by tumour thrombus. Renal failure produced a significant decrease in medullary perfusion ($p < 0.01$, Wilcoxon rank-sum test) with reduced cortical perfusion also, but not reaching statistical significance ($p = 0.07$). Renal cortical perfusion was significantly reduced in hypertension without captopril treatment when compared with normals ($p < 0.05$, Wilcoxon rank-sum test), whereas in hypertensives treated with captopril, cortical perfusion was not significantly different from normal. Hypertension and captopril had no effect on medullary perfusion.

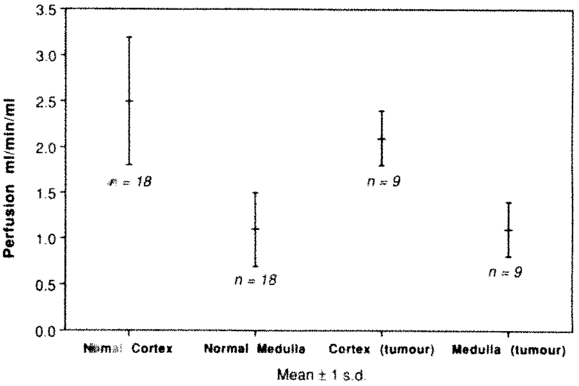


Figure 1. Mean values ± 1 standard deviation for cortical and medullary perfusion in normal kidneys and "normal" portions of tumorous kidneys.

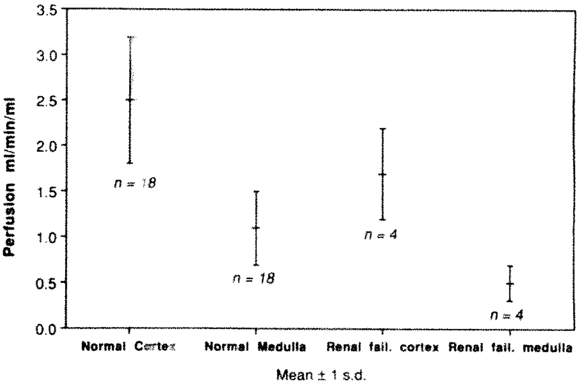


Figure 2. Mean values ± 1 standard deviation for cortical and medullary perfusion in normal kidneys and kidneys in patients with renal failure.

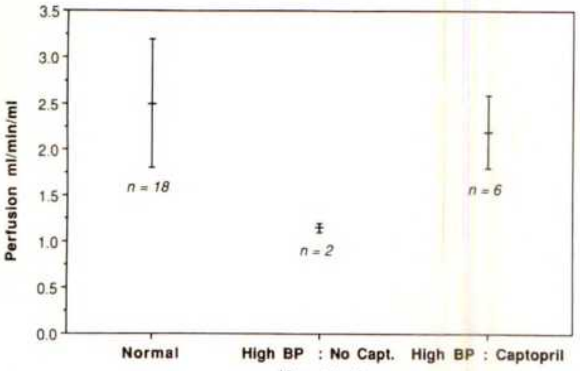


Figure 3. Mean values ± 1 standard deviation for cortical perfusion in normal kidneys and kidneys in patients with hypertension, with and without captopril.

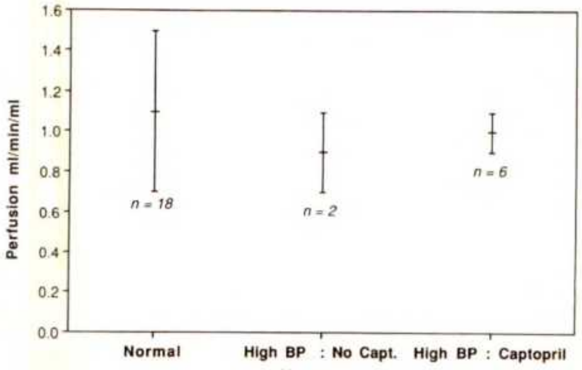
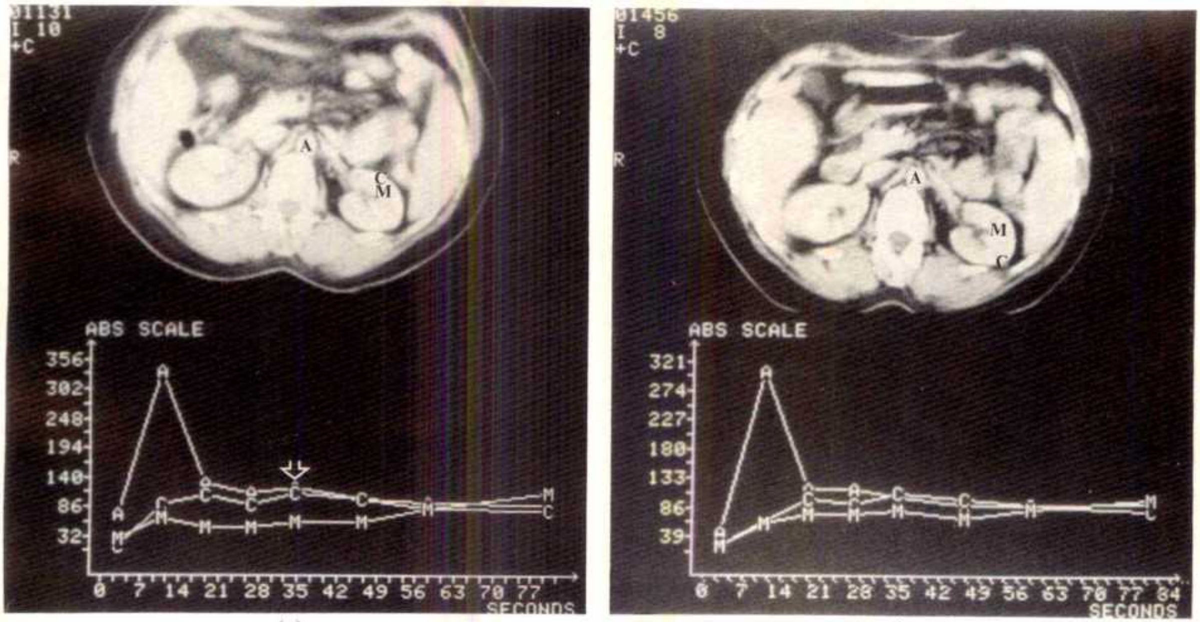


Figure 4. Mean values ± 1 standard deviation for medullary perfusion in normal kidneys and kidneys in patients with hypertension, with and without captopril.

Discussion

This study has shown that dynamic CT can provide quantitative functional information about tissue perfusion and that TDCs can be processed using nuclear medicine techniques. Quantitative functional information in the form of transit times has previously been derived from dynamic CT using deconvolution (Axel, 1983) and a semi-quantitative index of perfusion has also been described (Jansen et al, 1989), but absolute values for tissue perfusion from CT have not been previously reported. The technique is simple, requiring only the maximum slope of the tissue TDC and the peak enhancement in the aorta, and can be applied to most tissues. Changes with disease are seen indicating that the technique is potentially of value in diagnosis.

The value for splenic perfusion by CT of 1.2 ml min^{-1} ml^{-1} is close to the value of 0.96 ml min^{-1} g^{-1} obtained from intra-arterial xenon studies (Williams et al, 1968) and the standard deviation is similar. The higher value obtained from CT may reflect the vasodilatory effect of the contrast medium. Williams et al (1968) described an increase in splenic perfusion of 25% in one patient after intra-arterial contrast medium injection. Although non-ionic contrast



(a) (b)

Figure 5. Time–density curves from a hypertensive patient (a) with and (b) without captopril. (A = aorta, C = cortex, M = medulla. The arrow indicates the point of recirculation.) Note the increased slope of the cortical TDC after captopril.

medium, which is less vasodilatory, was used in these CT studies, this effect is likely to be of significance.

Other sources of error include the low sampling rate and the effects of photon noise. In these studies, the images were obtained every 6 seconds but newer machines have possible imaging rates of 1/second or less, which will reduce the problem but at the expense of greater radiation exposure. The main effect of low sampling rate will be underestimation of the height of the arterial curve and thus overestimation of the tissue perfusion. Photon noise was assessed for this machine by performing a dynamic scan sequence on a polythene phantom. An acceptable standard deviation of 3 HU during a seven-scan sequence was achieved with an ROI of 10 pixels. Thus, photon noise will not be significant for larger organs such as the spleen, but may become so for smaller ROIs. It is therefore important to keep ROIs as large as possible, whilst avoiding partial volume effects.

The mean value of 1.1 ml min^{-1} ml^{-1} for medullary perfusion in normal kidneys corresponds closely to the accepted value of 1 ml min^{-1} ml^{-1} derived from studies using intra-arterial xenon (Rosen, 1968) but the CT derived value of 2.5 ml min^{-1} ml^{-1} for cortical perfusion is significantly lower than the accepted value of 5 ml min^{-1} ml^{-1} (Rosen, 1968). Contrast agents are known to decrease renal blood flow (Russel & Sherwood, 1974) and this may account for the lower values obtained for the renal cortex. It should be remembered that the values obtained using xenon are derived using compartmental analysis, identifying a physiological rather than an anatomical compartment. To date, it has not been possible to study the renal cortex and medulla with separate anatomically defined regions and hence no true reference values are available.

The effect of contrast media on renal blood flow may be partially mediated by anti-diuretic hormone and the renin–angiotensin system (Trewhella et al, 1990). Renal cortical perfusion measured by dynamic CT was reduced in hypertension in keeping with the findings of Gruenewald (1980), but this reduction was reversed by captopril. It has been suggested that reduction in cortical blood flow may be the mechanism for contrast nephrotoxicity. This correction of cortical perfusion, as measured with contrast media and dynamic CT, is evidence that captopril is potentially of value in prevention of contrast medium nephrotoxicity—at least in patients where cortical perfusion is reduced, such as in hypertension, but also possibly in patients with renal failure, a high-risk group for contrast nephrotoxicity, where dynamic CT has demonstrated some reduction in cortical perfusion.

The ability of dynamic CT to provide quantitative functional information in addition to good anatomical detail is not well recognized. This method of determining tissue perfusion, applicable to most tissues, is of greatest potential benefit when the structures studied, such as the renal cortex and medulla, cannot be anatomically resolved by other functional imaging techniques.

Acknowledgment

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Doppler ultrasound studies in renal arteries of normal newborn babies

By A. C. Lamont, FRCR, H. S. Hall, J. R. Thompson, PhD and D. H. Evans, PhD, FInstP, FIPSM
Department of Radiology, Leicester Royal Infirmary, Leicester LE5 1WW, UK

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Abstract. The renal arteries of 89 healthy full-term infants were examined using duplex Doppler ultrasonography to establish a normal range for renal blood flow velocity in the first 3 days of life. In the first 24 h a wide range of renal blood flow velocities was noted with a statistically significant decrease in Pourcelot's index over the next 2 days.

Duplex Doppler ultrasound is a simple means of measuring blood flow in human neonates, and the cardiac circulation has been extensively studied (Wilde, 1989). Arterial studies have been confined mainly to the cerebral circulation (Evans et al, 1988; Levene, 1988). The study of blood flow velocity waveforms in the renal arteries of adults (Dubbins, 1986) and children (Keller, 1989; Wong et al, 1989) with Doppler ultrasound has proved most useful in kidney transplants (Slovis et al, 1984; Murphy et al, 1987; Ubhi et al, 1987; Stringer et al, 1989).

The changing Doppler pattern in the first few days of life has been described in the cerebral arteries (Archer et al, 1985; Drayton & Skidmore, 1986; Evans et al, 1988), the carotid arteries (Deeg & Rupprecht, 1988) and the superior mesenteric artery (Van Bel et al, 1990), but the changing pattern of neonatal renal blood flow, although previously investigated in animals, has not yet been established in humans.

The aim of this study was to find the normal range of renal arterial blood flow velocities in the first 3 days of life.

Methods

Prior approval for the study was obtained from the Leicester District Ethical Committee and signed consent was obtained. All examinations were carried out in the presence of at least one parent.

Pulsed Doppler recordings obtained from the renal arteries using the L558, 5 MHz linear transducer of an Acuson model 128 ultrasound scanner were made in digital form on magnetic tape. A minimum of five consecutive wave forms were collected and stored for processing.

In order to eliminate possible adverse effects of insonation of the neonatal renal artery and surrounding tissues, the output power of the Acuson scanner was pre-set to "low". At this setting the worst-case spatial peak temporal average (SPTA) intensity is 150 mW/cm^2 and the *in situ* value 34 mW/cm^2 (data from Acuson, 1989). The maximum exposure time for each kidney was 7.5 min, which is well within accepted safety limits (Evans et al, 1989).

The renal artery arises from the aorta at an angle θ° (90° to 45°). Therefore the kidney was first imaged longitudinally and θ° noted. The transducer was then rotated through 90° and angled cephalad by θ°, so that a transverse image of the kidney was seen with the renal artery vertically displayed and blood flow was directly towards the transducer. The Doppler sample area was positioned close to the hilum of the kidney. Adjustments were made to give a clear signal using both visual and auditory information and compensation was made for respiratory movement of the kidney (Fig. 1).

The studies were performed in a warm room with the infant relaxed, either asleep or eyes open with no gross movements (Prechtl & Beintema, 1964). The babies were wrapped in a small blanket, flank exposed, and lay on their sides in a cot or in their mothers' arms.

Two methods of extracting information from the Doppler signals were considered: analysis of the maximum frequency envelope (MFE) and analysis of the intensity weighted mean signal (IWM). The MFE was chosen for this study because of its greater immunity to noise. It was defined using a fast Fourier transfer analyser coupled to a computer (Gibbons et al, 1981; Schlindwein et al, 1988), and calibrated in terms of velocity using the Doppler equation.

The Doppler signals were analysed for:

(1) Peak systolic maximum flow velocity (PSMFV) in cm/s.
(2) End-diastolic maximum flow velocity (EDMFV) in cm/s.
(3) Pourcelot's pulsatility index (PI) was calculated according to the formula $PI = (S-D)/S$ where S and D are the maximum and minimum values of the maximum velocity envelope.

PSMFV, EDMFV and PI were plotted against the post-delivery age, Apgar score and body weight.

Address for correspondence: Department of Radiology, Leicester Royal Infirmary, Leicester LE1 5WW, UK.

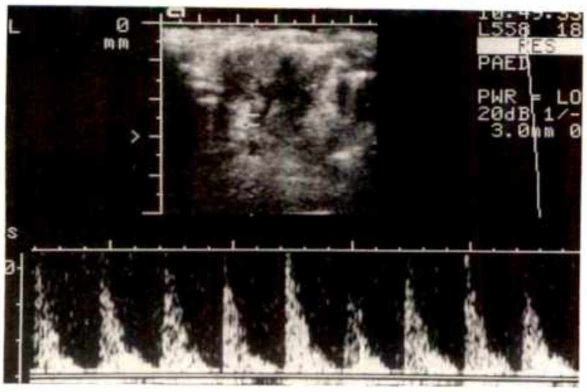

Figure 1. Renal arterial Doppler signal with duplex image showing the hilum of the kidney in tilted transverse section. The Doppler probe can be seen positioned over the renal artery, adjacent to the renal vein, with arterial blood flow directed towards the transducer.

Data were analysed using a bivariate linear regression, which allows for the correlation between values recorded on the right and left kidneys of the same infant at the same session, with modification to allow for missing data (Rosner, 1984).

Patients

During a 10-day period in February 1989 at the Leicester Royal Infirmary Maternity Hospital, 89 consecutive normal newborn babies (gestational age between 39 and 42 weeks) were examined between 1 and 3 days after birth. Eight infants were scanned on two occasions and two were scanned three times. Both kidneys were recorded on 77 occasions and only one kidney recorded in 17 instances. Satisfactory Doppler studies were obtained from a total of 171 kidneys. In only seven renal arteries were fewer than five consecutive Doppler wave forms obtained owing to excessive renal movement, and it was noted that in these cases the PI was not noticeably different from the contralateral side. They were therefore included in the study.

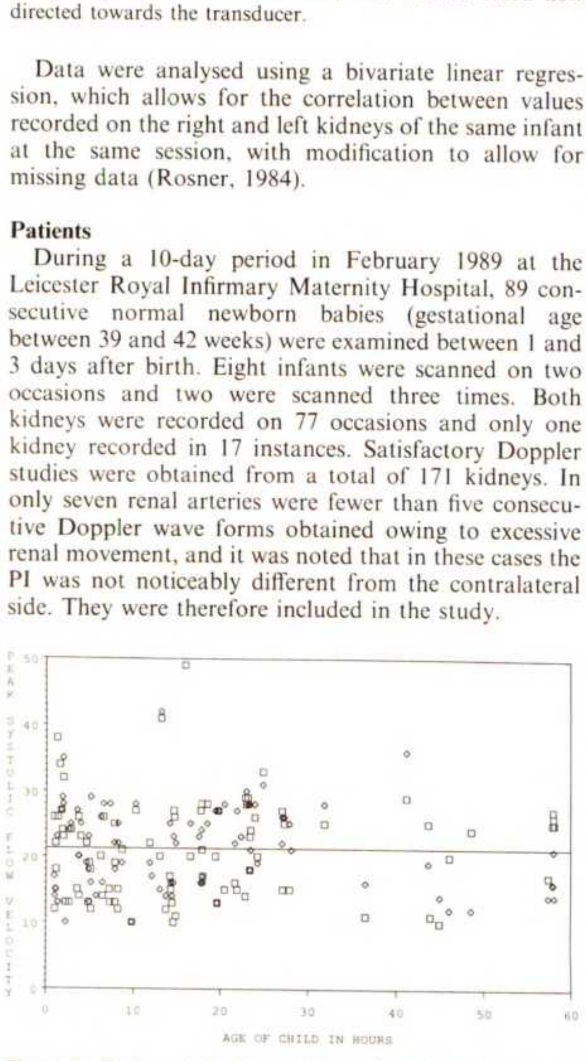

Figure 2. Peak systolic flow velocity plotted against age of infant in hours. The fitted trend is shown. Right kidney (□); left kidney (◇).

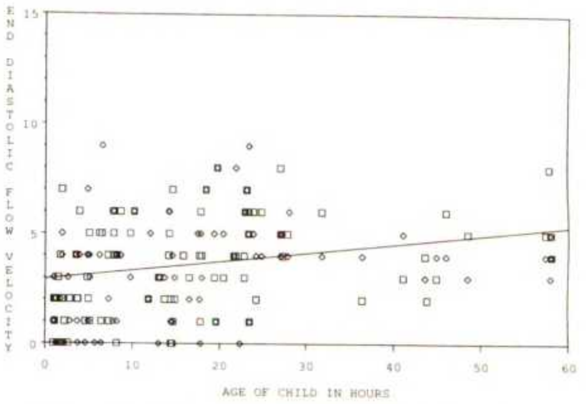

Figure 3. End-diastolic flow velocity plotted against the age of the infant in hours. The fitted trend is shown. Right kidney (□); left kidney (◇).

No information was obtained from 14 infants, not included in the study, owing to a temporary technical fault in the recording system and three further infants with congenital anomalies or pathological changes were excluded (two cases of unilateral hydronephrosis, and one duplex kidney). In these cases the parents and attending medical officer were informed.

Results

The PSMFVs showed no change over the period of study ($p = 0.73$) (see Fig. 2) and the average was found to be 21.2 cm/s (standard error (SE) 0.64 cm/s) with a standard deviation (SD) of 7.0 cm/s. Correlation between PSMFVs of the right and left kidneys was 0.52.

The EDMFV showed a rise over the period of the study ($p = 0.007$); the regression line was given by EDMFV = 2.94 + 0.0399 age in hours, where age ranged up to 60 h in this sample. Standard errors of these two coefficients were 0.33 and 0.014 (see Fig. 3). The correlation between the right and left kidneys was 0.62 and SD about the best-fit line was 0.787.

Pourcelot's index showed a constant fall over the period of the study, mirroring the EDMFV ($p = 0.001$); the regression line was given by PI = 1.861 − 0.00221 age, where the SE of these two coefficients were 0.15 and 0.00065 (see Fig. 4). Correlation between left and right side was 0.74 and SD about the best-fit line was 0.100.

Figure 5 shows the PI of 10 infants scanned on more than one occasion (left and right kidneys averaged), which confirms the general trend seen on the patients studied only once.

Birth weights and Apgar scores of the infants were also recorded, but no correlation was seen with the PI.

Discussion

In order to estimate absolute renal blood flow using Doppler, a precise measurement of the internal vessel diameter is critical. Any errors in calculation of the cross-section are doubled. This is the weakest link in the estimation of volumetric flow (Gill, 1985) and we felt

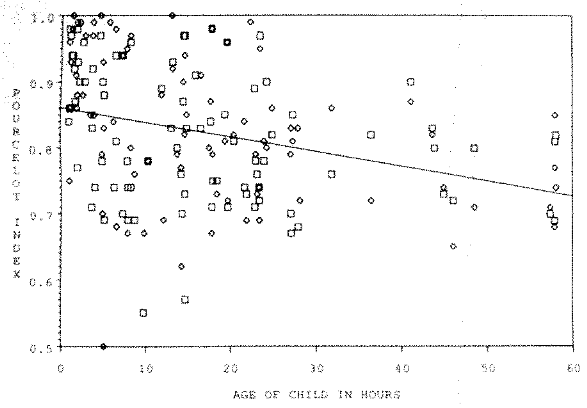

Figure 4. Pourcelot's index plotted against the age of the infant in hours. The fitted trend is shown. Right kidney (□); left kidney (◇).

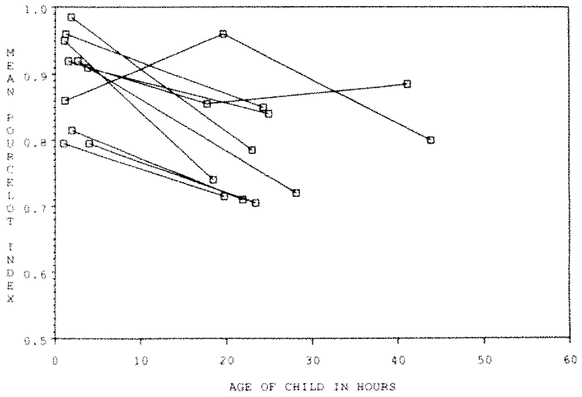

Figure 5. The mean Pourcelot's index of renal blood flow of both right and left renal arteries of 10 infants who were scanned on more than one occasion.

that direct measurements of the small neonatal vessels in our study were too inaccurate to be relied on. The measurement of PI, although it has some limitations, has been shown to have value for prediction of problems in the cerebral circulation of term infants (Archer et al, 1986).

The rapid turnover of otherwise healthy patients at this hospital meant that a longitudinal study of normal-term babies was not possible, most being discharged within 1 day. Great care was taken to ensure that only healthy full-term babies were studied and infants available beyond the initial 24 h period remained in hospital for maternal health or other social reasons. Although this study has the disadvantage of being largely cross-sectional, our trends are comparable to cerebral arterial studies in term infants by Drayton (Drayton & Skidmore, 1987).

We observed a wide spread of mean maximum renal arterial blood flow velocities at all ages. However, factors such as the varying state of arousal of the infants or the time since the last meal may have contributed to this. Correlation between right and left renal arteries was 0.74 suggesting that the range reflects biological distribution.

Mean systolic velocity remained constant over the 60 h observation period. However, diastolic velocity—and presumably, therefore, the mean renal arterial velocity—progressively increased. The mechanism for increase in renal arterial velocity is uncertain. Blood pressure, low at birth but progressively rising on average by 15 mmHg in the first 10 days of life (Bucci et al, 1972), has some effect but this is much smaller than observed changes. The PI was observed to fall with time, which may indicate localized renovascular dilatation or shunting distal to the Doppler sample site (Drayton & Skidmore, 1986, 1987; Wright et al, 1988). It is most likely that these circulatory changes can be explained by generalized physiological alterations within the renal vasculature and that the concomitant fall in PI could indicate distal renal vasodilatation. However, the effect of closure of a patent ductus arteriosis could possibly cause a decrease in PI, although none of the infants in this study had clinical evidence of PDA. This point was previously addressed in the cerebral arteries (Gentile et al, 1981; Perlman & Volpe, 1981).

In utero studies on fetal lambs have shown low renal blood flow associated with the output of a large volume of dilute urine, possibly due to reduced tubular sodium reabsorption (Robillard et al, 1981). At birth the kidneys are, even in full-term infants, histologically immature and subsequent maturation is relatively slow (Alexander & Nixon, 1961). They take over from the placenta primary regulation of fluids, electrolytes and excretion of potentially toxic substances. Concentrations of urine must be established almost immediately after birth to prevent excess fluid loss. These studies can be linked with other animal studies which indicate that within the first 12 h of life, renal vascular resistance falls by 50% (1.03 mmHg/ml/min to 0.5 mmHg/ml/min) (Gruskin et al, 1970; Aschinberg et al, 1975). This finding challenges the theory that intrarenal shunts close after birth and, as PI is related to peripheral vascular resistance (Evans et al, 1980; Skidmore et al, 1980), correlates well with our observations.

The appearance of the normal renal artery Doppler signal has been likened to a ski-slope. Its characteristics are those of a low-impedance vessel with continuous forward flow throughout diastole. Various diseases alter the resistance to flow through vessels either directly or indirectly. Attempts have been made to correlate measurements of these changes with the disease states. Most reports concentrate on Pourcelot's resistance index (PI) and the pulsatility index of Gosling (Nelson & Pretorius, 1988). Changes in the PI on Doppler studies should be readily detectable and if direct evidence of alteration to renal blood flow in high-risk infants can be made available, this would be extremely valuable (Daniel & James, 1976).

Duplex Doppler ultrasound of the renal arteries offers a non-invasive method for investigation of the blood supply to the kidney in the infant. It is important for the better understanding of the role played by disturbances in blood supply to the kidney and it may help in the monitoring of therapy.

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Non-ionic contrast media: a comparison of iodine delivery rates during manual injection angiography

[illegible] Hughes, MRCP, FRCR and *R. Bisset, MB BS, FRCR

Department of Radiology, Hope Hospital, Salford, Manchester, UK and *Department of Radiology, North Manchester General Hospital, Crumpsall, Manchester, UK

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Abstract. Iodine delivery rates (IDR) of five commonly used non-ionic contrast media were determined at room temperature (24°C) and body temperature (37°C). Contrast media of strength 300 mgI/ml were also evaluated at 50% dilution (150 mgI/ml) with N-saline. Iodine delivery differed significantly ($p < 0.005$) between samples at room temperature: Omnipaque 350 (1163 mg/s) < Niopam 370 (1311 mg/s) < Omnipaque 300 (1422 mg/s) < Niopam 300 (1635 mg/s) and Ultravist 300 (1636 mg/s). Niopam 300 and Ultravist 300 delivered 41% more iodine per second than Omnipaque 350 at room temperature. Similar differences were identified at body temperature, while delivery of individual media was on average 23.5% greater than at room temperature. No significant difference between iodine delivery rates of diluted media at room temperature or body temperature was identified. The results demonstrate that iodine delivery and hence vascular opacification are better achieved during hand-injection arteriography by using relatively low viscosity media such as Niopam 300 or Ultravist 300. In digital subtraction arteriography all 300 strength contrast media diluted to 150 strength are equally effective.

Contrast media injected at high velocity through fine bore catheters experience turbulent flow and therefore do not obey Poiseuille's law. Consequently, contrast viscosity and flow rates are not linearly related (Krovetz et al, 1966). Viscosity measurements offer the only objective evidence with which the ease of injection may be implied, but preclude comparison between contrast media of differing iodine content. When assessing the relative abilities of contrast media to produce vascular opacification it would seem more practical to compare the iodine delivery rates (IDRs) (Rees et al, 1988). These reflect more accurately the ability of a contrast medium to optimize image quality, particularly in high flow arterial systems where a tall, narrow time–concentration curve is essential (Becker et al, 1985). The rate of injection and iodine delivery may, however, be less important in slower flowing (venous) systems. We have measured iodine delivery rates for five non-ionic contrast media to determine which is most likely to produce optimum opacification during hand-injection angiography.

Method

Five non-ionic contrast media were evaluated (Table I). Those of 300 mgI/ml were also tested at half strength (50% dilution with normal(N)-saline). N-saline was employed as diluent as this was more frequently used than sterile water in the Manchester digital angiography units. Measurements were performed at ambient room temperature (RT) (24°C) and body temperature (BT) (37°C). Forceful hand in[illegible] ml of contrast medium were per[illegible] a 5F Headhunter catheter (No. 1) and injection times recorded. The timer consisted of a pair of infrared sources and detectors mounted in a fine plastic sheath into which a standard 10 ml syringe was placed. The sensors were triggered by the syringe plunger and injection times for 10 ml of contrast media recorded on a Quartz timer accurate to two decimal places. Contrast medium was stored in incubators at the predetermined temperatures. A single blind technique and random selection of contrast medium were used. Twenty test injections of each undiluted contrast agent and 30 test injections of each dilution were made by a single operator. The IDRs were calculated as a product of iodine concentration (mgI/ml) and flow rate (ml/s). The statistical evaluation was performed using two-factor analysis of variance and Tukey's critical range test.

Table I. Contrast media studied

Contrast medium	Viscosity (at 20°C) (mPa or cP)	Viscosity (at 37°C) (mPa or cP)
Niopam (N) 300 (Iopamidol)	8.8	4.7
Ultravist (U) 300 (Iopramide)	8.7	4.7
Omnipaque (O) 300 (Iohexol)	11.6	6.1
Niopam (N) 370 (Iopamidol)	18.5	8.6
Omnipaque (O) 350 (Iohexol)	23.3	10.6

Data from manufacturers' references.

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*Author for correspondence.

Table II. Mean contrast media injection times (10 ml contrast media)

Contrast medium	Injection times (±2SD) at room temperature (24°C) (s)		Injection times (±2SD) at body temperature (37°C) (s)	
N300	1.83	±0.07	1.52	±0.09
U300	1.83	±0.09	1.48	±0.09
O300	2.11	±0.13	1.71	±0.08
N370	2.82	±0.14	2.29	±0.13
O350	3.01	±0.28	2.37	±0.16

Results

The mean injection times (±2SD) for each medium, the IDRs (mg/s) and percentage differences between contrast agents at RT and BT are summarized in Tables II and III. With the exception of N300 and U300 there were statistically significant differences ($p < 0.005$) between the IDRs of the contrast media, the relative differences being similar at RT and BT. N300 and U300 demonstrated the most rapid iodine delivery, 41% more than O350 at RT and 37% at BT. The IDRs of N300 and U300 were 15% greater than that of O300 at RT and BT. Heating contrast media to BT significantly improved delivery rates by an average of 23.5% (range, 20% (N300) to 27% (O350)). The injection times and IDRs of diluted contrast media are summarized in Table IV. No significant differences between the IDRs could be demonstrated at either RT or BT. The coefficient of variance for the injection times was 4.9%.

Discussion

A knowledge of those factors influencing contrast medium delivery through catheter systems is required to optimize opacification and image quality in arteriography. As contrast media injected at high flow rates do not comply with Poiseuille's law, of more practical importance than viscosity in determining vascular opacification is the IDR (Fischer et al, 1964; Krovetz et al, 1966). The IDRs enable comparisons to be made between agents of differing iodine content. While the effects of temperature and viscosity on injection rates using pump injectors have been well documented (Fischer, 1965), hitherto to the authors' knowledge no study has considered their influence in hand-injection angiography. This method of delivery is commonly employed in both standard and digital imaging when pump injectors are either unsuitable or unavailable. We have determined the injection rates and IDRs of five common non-ionic contrast media using a 5 French catheter system to simulate conditions encountered during arteriography. Diluted media (50% N-saline) were also evaluated.

The results indicate that iodine delivery and hence vascular opacification is better achieved using N300 or U300 in preference to O300, O350 or N370. The differences in delivery between N300/U300 and O300 although statistically significant were small and unlikely to affect relative vascular opacification. N300 and U300 delivered approximately 40% more iodine per second than O350, in which case superior vascular opacification by the former is to be expected. Warming contrast media produced an average improvement in the IDR of 23.5%, twice that documented in previous studies on contrast delivery when pump injectors were used (Halsell, 1987; Rees et al, 1988). While the use of contrast agents at BT is physiologically advisable the results further justify warming to improve delivery.

Dilution of contrast media is a recognized method of reducing iodine concentration and viscosity (Dawson et al, 1983). N-saline is more often used than sterile water as a diluent as it is also used to flush catheter systems. Dilution increased the speed of injection, and despite this the average IDR was only 20% lower than that of undiluted agents. No significant differences between the IDRs of diluted contrast media at either RT or BT were identified. The absence of any improvement in iodine delivery on warming diluted contrast media is not unexpected as previous studies have shown heating to be mainly useful when high-viscosity contrast media are used in small bore catheters.

In summary, iodine delivery and hence vascular opacification during hand-injection angiography are better achieved using lower viscosity contrast media such as N300 or U300 at BT. All diluted 300 strength contrast media as used in intra-arterial digital subtraction imaging appear equally effective in terms of iodine delivery. It is hoped this study will improve our understanding of those factors governing vascular opacifica-

Table III. Iodine delivery rates and differences between contrast media

Contrast medium	IDR at 24°C		IDR at 37°C		Increased delivery, room temperature to body temperature
	mgI/s	%Increase in iodine delivered relative to O350	mgI/s	%Increase in iodine delivered relative to O350	
N300	1636	41%	1974	34%	20%
U300	1635	41%	2027	37%	24%
O300	1422	22%	1753	19%	23%
N370	1311	13%	1615	9%	23%
O350	1163	0%	1477	0%	27%

Table IV. Iodine delivery rates and injection times of diluted 300 strength contrast media (50% N-saline)

Contrast medium	At room temperature (24°C)			At body temperature (37°C)		
	IDR (mgI/s)	injection time (10 ml) (±2SD) (s)		IDR (mgI/s)	injection time (10 ml) (±2SD) (s)	
N300	1258	1.19	(±0.5)	1271	1.18	(±0.4)
U300	1267	1.18	(±0.5)	1280	1.17	(±0.6)
O300	1273	1.18	(±0.7)	1268	1.18	(±0.8)

tion, allowing a more informed selection of contrast medium when performing manual angiographic procedures.

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Is the coned lateral lumbosacral junction radiograph necessary for radiological diagnosis?

By M. E. Lipton, FRCR, V. Pellegrini, FRCR and I. Harris, FRCR

Department of Radiology, Royal Liverpool Hospital, Prescot Road, Liverpool, UK

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Keywords: Lumbosacral junction, Coned lateral radiograph, Diagnosis

Abstract. The lumbar spine radiographs of 400 orthopaedic outpatients were reviewed to determine if the absence of the coned lateral lumbosacral junction radiograph would lead to a loss in diagnostic accuracy. In 84 (21%) patients the antero-posterior and lateral lumbar spine radiographs failed to visualize adequately the lumbosacral junction. In these patients the coned lateral lumbosacral junction radiograph resulted in 17 (4.5%) diagnoses which would otherwise have been missed. The diagnoses were spondylosis (11), spondylolisthesis (3), spondylolysis (1), Paget's disease (1) and infection (1). Absence of the coned lateral lumbosacral radiograph will result in inadequate demonstration of the lumbosacral junction and a loss in diagnostic accuracy.

In many clinical situations, reduction in routine sets of radiographs is being advocated. However, such changes in radiological practice must not result in loss of diagnostic accuracy. The plain radiograph examination of the lumbar spine is one area recently under review. The aim of this study was to assess whether the absence of the coned lateral lumbosacral junction (LSJ) radiograph would lead to a loss in diagnostic accuracy.

Method

A total of 400 patients referred from orthopaedic outpatients for plain radiographs of the lumbar spine were reviewed. A routine examination was performed on each patient which included anteroposterior (AP), lateral and coned lateral LSJ radiographs. The radiographs were reported on two occasions a fortnight apart. On the first occasion a report was issued on all three radiographs. On the second occasion the AP and lateral radiographs were only reported and the difference between the reports noted. The lateral radiograph was also assessed for the visualization of the LSJ. This was defined as adequate (Grade 1) with full visualization of the inferior end plate of L5 and the superior end plate of S1, not visualized (Grade 3) or intermediate (Grade 2).

Results

The LSJ was inadequately seen in 84 (21%) patients with the AP and lateral radiographs only (Table I). In 17 patients (4.25%) diagnoses were made from the coned lateral LSJ radiograph (Table II), of which 15 were made despite partial visualization of the LSJ on the lateral radiograph.

Table I. Visualization of the LSJ on AP and lateral radiographs

Assessment	Number	%
Grade 1	316	79.0
Grade 2	55	13.8
Grade 3	29	7.2
Total	400	

Table II. Diagnoses made on coned lateral LSJ radiographs with assessment of the LSJ on AP and lateral radiographs only

Diagnosis	Number	Grade
Spondylosis	10	2
	1	3
Spondylolisthesis	2	2
	1	3
Spondylolysis	1	2
Paget's disease	1	2
Infection	1	2
Total	17	

Discussion

Eisenberg et al (1979) suggested that a single lateral radiograph centred 1 cm above the iliac crest would give adequate visualization of the LSJ. However, the study included only 30 patients and no reports have been published of this technique in a large department. Padley et al (1990) suggested a lateral radiograph only would be adequate for their population. However, 4% of the LSJs were not visualized. Their population was made up of screened GP referrals of "back pain" unlike ours which were unscreened orthopaedic outpatients. Pathology is greater in our population and hence poor visualization of the LSJ leads to a greater incidence of missed diagnosis. As Butt (1989) commented on those studies advocating reduced plain film radography: "One

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Address correspondence to Dr M. E. Lipton, Radiology Department, Alder Hey Hospital, Eaton Road, Liverpool L12 2AP, UK.

would need reassurance that the patients studied were not primarily those where no useful purpose would be served by any type of radiology."

Our results demonstrate the need for adequate visualization of the LSJ in plain radiographs of the lumbar spine. In our population, if full visualization of the LSJ was not present there would be a significant loss of diagnostic accuracy. Any alteration in the standard set of radiographs of the lumbar spine must not occur at the expense of inadequate visualization of the LSJ.

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Lymphography—current role in oncology

By E. Moskovic, MRCP, FRCR, *I. Fernando, BSc, MRCP, *P. Blake, MD, FRCR and C. Parsons, FRCS, FRCR

Departments of Radiology and *Radiotherapy, The Royal Marsden Hospital, Fulham Road, London SW3 6JJ, UK

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Keywords: Lymphography, Computed tomographic scanning, Magnetic resonance imaging, Ultrasound, Lymph nodes, Neoplasm, Lymphoma, Cervix, Testis, Ovary, Prostate, Bladder

Abstract. A review of the use of lymphography at this hospital, a major oncology centre, is presented. The advent of computed tomography has brought a dramatic reduction in the number of lymphograms currently performed for diseases such as lymphoma, testicular tumours and gynaecological malignancies. This study analyses the reasons for this decline, and concludes that valuable information can still be obtained from lymphography in certain selected groups of patients.

The number of lymphograms performed in oncology centres has declined markedly since the introduction of cross-sectional imaging techniques, particularly computed tomography (CT) (Castellino & Marglin, 1982; Choyke et al, 1985; Dixon, 1985; Dooms & Hricak, 1986; Lewis, 1987). The present study was undertaken in order to assess whether this trend is justified, and to determine any residual use for lymphography in the investigation and follow-up of cancer patients.

Methods

The requirement for bipedal lymphography at the Royal Marsden Hospital (London) in the decade from 1980 to 1989 inclusive was reviewed retrospectively both in total and also by recording the number of lymphograms in each of the major cancer disease groups. Computed tomography became available to this branch of the hospital in 1984.

The current clinical usefulness of lymphography in the presence of CT (*i.e.* its impact on therapeutic decision-making and follow-up) for each of the major disease categories has been assessed, using data both from this hospital and from a review of the recent medical literature.

Results

The decline in the number of lymphograms carried out at this cancer centre during the 1980s is shown in Fig. 1. The total number of lymphograms performed in 1980 at this hospital was 536. In 1984, the year that CT was introduced, the number had fallen to 458, and by 1989 the yearly total of lymphograms was 101, less than one fifth of the number performed in 1980.

Figure 2 illustrates this numerical information by disease. In 1980, nearly 40% of the yearly total of lymphograms were performed on patients with lymphoma, with gynaecological malignancies accounting for the bulk of the remainder: cervix 20%, ovary 20%, and endometrium 10%. Urological tumours including testicular cancers made up just over 10%. By 1989, when CT had been on site for 5 years, only 101 lymphograms were undertaken in total and the breakdown of this figure by disease had changed radically (see

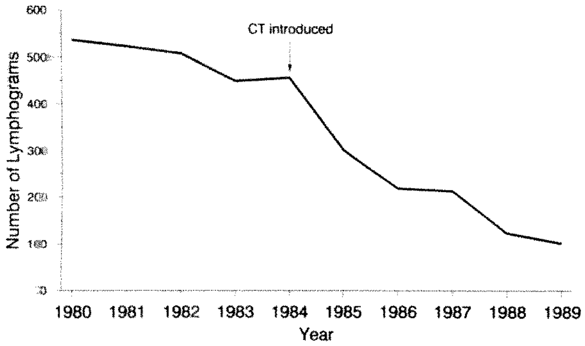

Figure 1. Number of lymphograms at the Royal Marsden Hospital, 1980–1989.

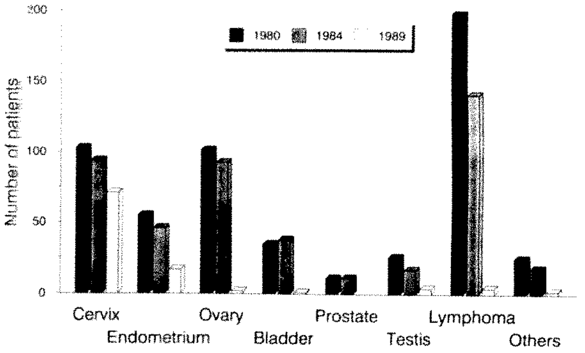

Figure 2. Number of lymphograms by disease, 1980–1989.

Address for correspondence: Dr E. Moskovic, Senior Lecturer, Department of Radiology, The Royal Marsden Hospital, Fulham Road, London SW3 6JJ, UK.

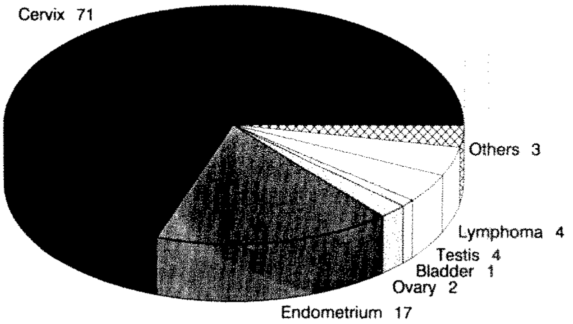

Figure 3. Number of lymphograms by disease, 1989.

Fig. 3). Lymphoma accounted for only 4% of investigations, whilst gynaecological tumours represented 90% of the total: cervix 70%, endometrium 17%, and ovary 2%.

The vast majority of lymphograms performed in 1989 in this hospital, therefore, were on patients with gynaecological malignancies, with carcinoma of the cervix accounting for 70%. Analysis of the impact of the information provided by lymphography in each of the gynaecological malignancies at this hospital suggests that only in carcinoma of the cervix can lymphography contribute to useful management decisions. This has been suggested in previous publications from this institution (Page et al, 1988; Graham et al, 1989). A review of radiological data from 100 patients with carcinoma of the cervix at this hospital showed that five of 34 patients with clinical stage IB disease had pelvic and/or para-aortic lymphadenopathy demonstrated on lymphography, following normal CT (Fernando et al, in preparation). This finding spared these patients unnecessary surgery, in favour of radiotherapy, and their subsequent survival has been significantly poorer than their lymphogram-negative counterparts.

Discussion

Selection of appropriate imaging techniques in the staging of patients with malignancy requires consideration of a number of factors beyond a sound knowledge of the pathology and behaviour of individual diseases, their modes of spread and sites of relapse. Whilst the accuracy, sensitivity and specificity of a diagnostic test are clearly important, other issues such as the availability of equipment and expertise, degree of invasiveness of the test, its cost, medical contraindications, and the preferences of both the radiologist and clinician involved must be appreciated. Of paramount importance is whether the result of the investigation undertaken in the presence of all other diagnostic information available will influence the staging of a disease and its subsequent treatment.

The introduction of cross-sectional imaging, in particular CT, has radically altered imaging protocols in oncology over the last 10 years, providing detailed anatomical information not available using previous techniques (Dixon, 1985). This is particularly relevant in abdominopelvic malignancy including the lymphomas, where detection of disease within retroperitoneal and pelvic lymph nodes had previously relied on lymphography. Technically, lymphography is more invasive than CT, requiring a cut-down to both feet, the injection of patent blue dye, and the infusion of an oil-soluble contrast medium into the lymphatics, all of which carry a small morbidity owing mainly to allergic reactions to the blue dye and pulmonary oil embolism (Kinmonth, 1982; Whitehouse & Worthington, 1983). Computed tomography has a clear advantage in being able to visualize consistently nodes not opacified by lymphography (so-called "off-axis" nodes, *i.e.* internal iliac groups, nodes within the mesentery, hepatic porta and splenic hilum and also those above the diaphragm) and of course other organs. It carries no significant morbidity, takes less time overall to perform than lymphography, but is more expensive; the implementation of a "capital charging" system under the NHS review will underline the fact that investigations performed on high capital value equipment such as a CT scanner necessarily cost more than those requiring a low initial outlay such as lymphography.

Whilst neither CT nor lymphography can detect the presence of micrometastases within lymph nodes (a major source of false-negative investigations), only lymphography is able to discern malignant involvement within nodes which are not enlarged and appear normal on CT. The unique ability of lymphography to evaluate internal architectural derangements within such nodes makes it diagnostically more accurate than CT in these circumstances, and this has led many centres to reserve lymphography only for investigating patients with negative CT in selected diseases (Castellino & Marglin, 1982; Choyke et al, 1985; Dixon, 1985; Castellino, 1986; Dooms & Hricak, 1986; Reznek & Richards, 1987). In a recent review of 92 published studies, all with histopathological correlation comparing the diagnostic accuracy of imaging malignant lymph nodes in the thorax abdomen and pelvis, Dooms and Hricak concluded that overall whilst lymphography was slightly more accurate than CT in diagnosing lymphomatous involvement of abdominopelvic lymph nodes (85% versus 81%), for testicular malignancies and other pelvic carcinomas the accuracies were equal at around 80% (Dooms & Hricak, 1986).

The key question is therefore whether lymphography is justified in the investigation of patients with node-negative CT, and whether by altering the clinical stage of disease it may substantially alter the patient's management and outlook. Clinical interest in lymphography at this institution has undoubtedly decreased in the disease categories for which modern chemotherapy has a high success rate (see Figs 1–3). These diseases include testicular tumours, lymphoma, and to some extent ovarian carcinoma, all of which we now stage solely by CT, with minor exception. Serum tumour markers have also become increasingly important adjuncts in the investigation and management of testicular and ovarian tumours. In pelvic malignancies such as carcinoma of the cervix where the only chance of cure is via radical surgery or radiotherapy, lymphographic information on precise nodal status beyond the resolution of CT may still be valuable, if only to avoid futile surgery.

The lymphomas

Analysing the use of lymphography by disease at this hospital, reveals that lymphoma accounted for over 200 (40%) of the total number of procedures in 1980 with only four (less than 4%) performed in 1989. Traditionally, lymphography provided the "gold standard" for staging both Hodgkin and non-Hodgkin lymphoma, owing to its ability to interrogate normal sized or minimally enlarged nodes which display either focal filling defects or a typical diffuse reticular or "foamy" appearance when involved (Marglin & Castellino, 1981; Kinmonth, 1982; Bragg et at, 1985). The accuracy of lymphography in assessing on-axis nodes in abdominopelvic lymphoma is undoubtedly superior to CT and, as previously mentioned, various studies support this finding (Castellino, 1986; Dooms & Hricak, 1986; Strijk, 1987). However, disease in non-Hodgkin lymphoma is often manifested at presentation with large lymph nodes involving widespread nodal groups and visceral involvement; it is easily evaluated by CT and lymphography provides no additional or unique information (Neumann et al, 1983; Bragg et al, 1985, 1986; Pond et al, 1989). Non-Hodgkin lymphoma is usually treated by chemotherapy rather than radiotherapy. In Hodgkin disease, the presentation is usually earlier, often supradiaphragmatic, with spread occurring predictably from one nodal group contiguously to the next. Involved nodes are smaller in size than in non-Hodgkin lymphoma and may often appear normal on CT (Bragg et al, 1985; Castellino, 1986). These factors can still make a case for performing lymphography on patients with Stage II (*i.e.* abdominopelvic CT-negative) supradiaphragmatic Hodgkin disease, particularly if curative radiotherapy to the mediastinum is being considered (Castellino, 1986). This strategy, however, whilst popular in the USA, is no longer routinely adopted in this hospital; accuracy of abdominopelvic CT is high (albeit not as high as lymphography in this situation), and, if understaged, successful salvage by chemotherapy is often curative (Bragg et al, 1985; Castellino, 1986). Computed tomography can also assess extranodal disease, although its diagnostic accuracy in early small-volume hepatosplenic disease is poor (Castellino et al, 1984; Castellino, 1986). Protocols for follow-up of patients after treatment for Hodgkin lymphoma are also controversial; proponents of lymphography stress the ease, cheapness and accuracy of a single plain abdominal film, which can detect relapse before clinical evidence of relapse in 30%, and at the same time as is evidenced clinically in a further 30%. Those in favour of CT remind us that diagnostic levels of lymphographic contrast only remain within opacified nodes for 12–18 months, and that 50% of relapses occur after this interval (Lee et al, 1980; Bragg et al, 1985; Castellino, 1986; Pera et al, 1987; Reznek & Richards, 1987). Lymphography no longer has a role in the staging of paediatric lymphoma (either at this institution or elsewhere), having been largely superseded by CT (Cohen et al, 1986).

Cervical carcinoma

The gynaecological malignancies accounted for 90% of the total number of lymphograms performed at this institution in 1989; most (70%) were for carcinoma of the cervix. Lymphography is routinely performed as an adjunct to CT in this hospital in patients with clinical stage IB and IIA disease, prior to consideration for Wertheim's hysterectomy. Our review of the lymphograms and CT scans of 100 patients with cervical carcinoma has shown that 15% of cases with stage IB disease (five of 34) had lymphographic evidence of small-volume nodal involvement, not demonstrated on CT, which directly altered their subsequent management to that of radiotherapy. Although the presence of lymph node metastases does not change the clinical stage, it is well known that survival and disease-free interval in carcinoma of the cervix are considerably shortened by the presence of positive nodal involvement (Bragg et al, 1985; Alcock & Toplis, 1987; Haie et al, 1988). Our experience supports this; the outcome for this albeit small group of patients was significantly worse than that for the node-negative stage IB patients, suggesting that lymphography can usefully alter therapeutic decision-making in this disease. Other authors remain divided on this issue. Not surprisingly, the level of lymphographic accuracy is higher in institutions where more examinations are performed, and this will add bias to local clinical and radiological preference (Ginaldi et al, 1981; de Muylder et al, 1984; Smales et al, 1986; Vercamer et al, 1987; Swart et al, 1989).

Other gynaecological malignancies

The role of lymphography in the postoperative management of carcinoma of the endometrium at this hospital was recently reviewed by Graham and his colleagues (Graham et al, 1989). They analysed 57 consecutive cases, 85% of which had undergone lymphography, and concluded that in no case did the result of the lymphogram alter management. Relapse occurred in four patients (one, pelvis alone, two, pelvis and lung; one, lung alone), all of whom had normal lymphograms at initial staging. The most important prognostic factor in this disease is the histological grade of the tumour; lymphography for endometrial carcinoma has subsequently been abondoned at this institution; none has been performed for this condition during this year (1990).

Lymphography also has no role in the investigation of the vast majority of ovarian tumours, 85% of which are epithelial in type and spread predominantly by direct extension to surrounding structures, with a marked tendency to shed malignant cells into the peritoneal cavity. Therefore, although significant spread to both pelvic and para-aortic nodes has been found to occur in all stages, carcinoma of the ovary should be regarded as a disease of the entire peritoneal cavity for which CT is the imaging modality of choice (Castellino & Marglin, 1982; Bragg et al, 1985; Lewis, 1987). The only potential role for lymphography in ovarian malignancy is in the investigation of ovarian dysgerminoma, which behaves in a similar fashion to testicular seminoma, metastasizing primarily via the lymphatics to the para-aortic nodes (Santoni et al, 1986; Piver, 1987). However, we recommend CT as the first method of investigation for this tumour, with lymphography perhaps reserved for CT-negative cases.

Testicular tumours

Although testicular tumours metastasize commonly via the lymphatics to the para-aortic nodes, lymphography is no longer used routinely for staging. Despite the value of lymphography in demonstrating metastases in normal sized nodes, CT is superior to lymphography overall in staging and follow-up of testicular tumours, and it is also valuable in demonstrating the relationship of nodal metastases to important structures such as the renal vein prior to para-aortic node dissection (Marincek et al, 1983; Williams et al, 1987; Gelderman et al, 1989; Williams and Husband, 1989). Some centres routinely employ lymphography in CT-negative patients, particularly in seminoma, for which the primary treatment is radiotherapy rather than chemotherapy for metastatic nodal disease (Desprez-Curely, 1985; Taylor et al, 1986). Harding and his colleagues in Glasgow have recently shown that performing lymphography on CT-negative patients with testicular teratoma confers no significant long-term benefit, and the procedure there has been abandoned (Harding et al, 1990). In the detection of relapse of testicular malignancy, lymphography has been shown conclusively to be inferior to CT, particularly when it occurs after 12 months from initial diagnosis. This is due mainly to failure of nodes to retain lymphographic contrast, and also because extranodal relapse cannot be visualized (Williams et al, 1987; Williams & Husband, 1989).

Carcinoma of the bladder and prostate

The lymphatic drainage of the bladder is first to the perivesical, and then to the obturator and internal iliac group of nodes; these are the nodes which bipedal lymphography fails to opacify, and this, combined with the ability of CT to evaluate the primary tumour, has led to a preference for CT in the initial staging of bladder cancer both at this hospital and elsewhere (Bishop, 1985; Bragg et al, 1985). Lymphography is no longer used prior to radical cystectomy in patients with node-negative CT in this institution; such patients in whom lymphadenectomy proves positive at cystectomy receive post-operative radiotherapy.

Lymphography has not been performed in significant numbers for prostatic cancer at any time over the past 10 years at this centre. Although prostatic carcinoma frequently metastasizes to regional lymph nodes, as with bladder cancer, early spread to the internal iliac and obturator groups will not be demonstrated by bipedal lymphography. Also, the prognostic significance of positive nodal status in prostatic cancer has been questioned by various authors; other factors such as patient age and degree of tumour differentiation appear to be more important in terms of overall survival (Pilepich et al, 1987; Castellino, 1988; Perez et al, 1989). Radical prostatectomy is performed on selected patients with prostatic carcinoma in the USA; this uses lymphography as an adjunct to the assessment of nodal status in patients with node-negative CT (Castellino, 1988). A small number of patients at this hospital have recently started undergoing this form of investigation and therapy, the results of which will be appraised.

Ultrasound and magnetic resonance imaging

Reference should be made to the current role of other cross-sectional imaging modalities in the evaluation of nodal disease in abdominopelvic malignancy. Ultrasound provides a cheap, accessible, non-invasive and sensitive primary method of investigating patients with an abdominal or pelvic mass. However, the presence of bowel gas often precludes adequate evaluation of the entire retroperitoneum, and image resolution is degraded by subcutaneous and retroperitoneal fat in an obese patient. Ultrasound is less precise than CT in the detection of lymph nodes smaller than 2 cm in diameter, and overall, CT has been shown to be more accurate for staging purposes in all the major disease categories mentioned (Bragg et al, 1985; Dooms & Hricak, 1986; Reznek & Richards, 1987). Currently, outside neuroradiology, magnetic resonance (MR) imaging is not widely available for clinical use in this country, and its role in investigating and monitoring patients with abdominopelvic malignancy is still under review. However, various recent MR studies have shown high degrees of accuracy in delineating local extent of tumour in pelvic malignancies such as carcinomas of the bladder, prostate and cervix. The advantages of MR over CT include non-invasiveness, better contrast resolution and the facility of multiplanar images, in particular sagittal views (Lee et al, 1984; Bryan et al, 1986; Dooms & Hricak, 1986; Fishman-Javitt et al, 1988; Greco et al, 1989; Johnson et al, 1990; Kim et al, 1990). In common with CT, MR cannot detect disease within normal size lymph nodes, and at present it is less accurate than CT in defining disease within the upper abdomen and retroperitoneum because of bowel motion artefact due to longer scanning times, lack of available bowel contrast and poorer spatial resolution. As more technological advances are made, MR is likely to have a greater impact on imaging strategies in abdominopelvic oncology.

Conclusion

This study has documented a justifiable decline in the use of lymphography in oncology for most of the major disease categories described. There remain certain situations in which this technique still has a role when CT is negative for nodal disease. These comprise patients with stage IB carcinoma of the cervix being considered for

Wertheim's hysterectomy, and in special circumstances, the staging of some Hodgkin lymphomas for which radiotherapy alone is the proposed treatment. A small number of patients being assessed for radical prostatectomy will also be included as this operation becomes more widespread. These indications are likely to be controversial since current imaging practices vary widely. However, there is no doubt that given the declining use of this technique, levels of future expertise both in performing lymphography and in its interpretation will fall.

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Implications of the uptake of ^{131}I-radiolabelled meta-iodobenzylguanidine (mIBG) for the targeted radiotherapy of neuroblastoma

By *†§J. A. O'Donoghue, BSc, PhD, *†§T. E. Wheldon, BSc, PhD, ‡J. W. Babich, BSc, MSc, RPh, ‡||J. S. E. Moyes, MA, MB, FRCP, *§A. Barrett, MD, FRCR and ‡S. T. Meller, MB, FRCP

*Radiation Oncology Research Group, Beatson Oncology Centre, Belvidere Hospital, London Road, Glasgow G31 4PG, †West of Scotland Health Boards, Department of Clinical Physics & Bio-engineering, 11 West Graham Street, Glasgow, G4 9LF, and ‡The Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT, UK

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Abstract. Selective uptake of radiolabelled meta-iodobenzylguanidine (mIBG) in neuroblastoma provides a possible approach to biologically targeted radiotherapy of this disease. A mathematical model was used to predict absorbed doses to tumours of varying size from therapeutic ^{131}I-mIBG, based on measurements of ^{125}I-mIBG uptake in surgically excised tumours from six patients. Two size categories of tumour target were considered: bulk tumour and microscopic disease. The predicted absorbed doses were compared with doses calculated to achieve a 50% probability of tumour cure. The analysis shows that the probability of tumour cure depends strongly on mIBG uptake, effective half-life of mIBG in tumour and tumour diameter. Small microtumours may be relatively resistant to mIBG treatment owing to the limited absorption of ^{131}I beta-energy. The product of patient mass and percentage uptake per unit mass of tumour may be a useful indicator of therapeutic outcome when targeted radiotherapy is used for the treatment of paediatric tumours.

Neuroblastoma is prone to early dissemination, with at least 50% of children first diagnosed with advanced disease. Despite complete remission rates of 60–70% after chemotherapy for systemic neuroblastoma, relapse occurs in up to 80% of patients. Some of these will have had detectable residual abdominal disease following chemotherapy, but others will have had no evidence of residual disease. There is thus a need for effective consolidation of remission. To this end the use of "megatherapy" (high-dose chemotherapy and/or total-body irradiation followed by autologous marrow rescue) has been studied (Philip et al, 1985).

Another possible approach is biological targeting of neuroblastoma with a cytotoxic agent. The pharmaceutical meta-iodobenzylguanidine (mIBG) labelled with the radionuclide ^{131}I has been used as a method of treatment to reduce the relapse rates in both the above patient categories (Hartmann et al, 1988; Lashford et al, 1988; Moyes et al, 1989; Treuner et al, 1988).

This paper describes a mathematical model study of the use of ^{131}I-mIBG for systemic radiotherapy of neuroblastoma. In particular, the predicted therapeutic consequences of recent data on mIBG uptake by tumours are examined. Moyes et al (1989) have reported the quantitative uptake of mIBG by human neuroblastoma in six patients for whom administration of low activities of radiolabelled mIBG preceded surgical removal of tumour. In the present paper the likelihood of tumour cure by mIBG therapy for these patients is assessed. Additional published data on mIBG whole-body clearance kinetics, together with standard dosimetric methods, are used to calculate predicted absorbed doses to tumours of varying size. Target tumours are considered as falling into one of two classes:

(1) Macroscopic tumours of sufficient size that electronic equilibrium conditions apply, *i.e.* the energy absorbed within the tumour is equal to the disintegration energy emitted by radionuclides in the tumour volume. For the radionuclide ^{131}I this occurs for tumours with diameters greater than or equal to approximately 2 cm.
(2) Microscopic disease; in this case, for tumours of 2 cm diameter or less, electronic equilibrium is not achieved, *i.e.* a proportion of the disintegration energy from radionuclides within the tumour escapes from the tumour boundaries. The smaller the tumour the higher the proportion of disintegration energy that escapes, *i.e.* the absorption of radionuclide disintegration energy is size dependent

The predicted absorbed doses were compared with doses calculated to achieve a 50% probability of tumour cure.

Address correspondence to Dr J. A. O'Donoghue.

§Current address: Beatson Laboratories, Department of Radiation Oncology, Alexander Stone Building, Garscube Estate, Bearsden, Glasgow G61 1BD, UK.

||Current address: Department of Paediatric Oncology, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE, UK.

This enabled the likely therapeutic efficacy of mIBG to be assessed, and identified possible means by which it may be improved.

Mathematical model for tumour sterilization by ^{131}I-mIBG

The model study consists of two parts: (a) the calculation of doses required for a 50% probability of tumour cure, and (b) the calculation of absorbed dose to tumours based on mIBG uptake. The amount of injected activity of ^{131}I-mIBG was chosen to produce a mean whole-body dose of 2 Gy for each patient (*i.e.* varies from patient to patient depending on body weight), which is judged to be within the tolerance of the haemopoietic system. These doses are then compared to predict the estimated therapeutic efficacy.

Doses required for tumour cure

On the basis of a simple Poisson model the dose required for a certain probability of cure for a tumour depends only on the initial number of clonogenic tumour cells present and their radiosensitivity. In this study it was assumed that the radiation survival curve for neuroblastoma cells is a simple exponential with a slope given by $1/D_0$. For an exponential survival curve D_0 is the mean lethal dose and may be defined as the dose required to give a surviving fraction of e^{-1} or 0.37. It was further assumed that a proportion, k, of tumour cells are clonogenic and that there is no proliferation of tumour cells throughout the course of treatment by mIBG. With these assumptions it is shown in Appendix 1 that:

$$D_P = D_0 \ln\{kf(d_t/d_c)^3/\ln(1/P_c)\} \tag{1}$$

where D_P = dose required for a probability P_c of cure; f = packing factor, *i.e.* the proportion of the tumour volume consisting of tumour cells; d_t = tumour diameter; and d_c = average diameter of a tumour cell.

Dosimetric model

The dosimetric model presented here is based on the MIRD formalism (Dillman and von der Lage, 1975; Loevinger and Berman, 1976). Tumour doses from ^{131}I-mIBG therapy were calculated assuming that the uptakes measured in bulk tumours (see Sources of Data) are also applicable to micrometastases. The whole-body clearance kinetics of mIBG are assumed to be bi-exponential with the first component being very fast and contributing little to dose (see Sources of Data). No attempt was made to assess the effects of non-uniform radionuclide deposition in the tumour. With these assumptions, it is shown in Appendix 2 that the absorbed dose to a tumour is given by the following expression:

$$D_T = k_t/\lambda_t + k_b/\lambda_b \tag{2}$$

where $k_t = A_0 u_0 \phi D_\beta$ and $k_b = A_0 F(mS - \phi D_\beta)/m$.

The meanings of these quantities are: A_0 = initial injected activity (in MBq); u_0 = initial uptake per gram of tumour; ϕ = absorbed fraction of β-energy for the tumour (= 1 for bulk tumour, *i.e.* $\geqslant$ 2 cm diameter); D_β = equilibrium β-dose constant for ^{131}I; $\lambda_t = \ln 2/T_{\frac{1}{2}}$; where $T_{\frac{1}{2}}$ = effective half-life of ^{131}I bound to tumour = $(T_{\text{biol}} T_{\text{phys}})/(T_{\text{biol}} + T_{\text{phys}})$; T_{biol} = biological half-life of ^{131}I bound to tumour; T_{phys} = physical half-life of ^{131}I; F = proportion of the initial activity lost from the whole body through the second component of the bi-exponential clearance; m = patient mass; $S = S_{\text{WB-WB}}$ the absorbed dose to the whole body per unit cumulated activity in the whole body (in Gy/MBq h). This factor depends on the patient mass; $\lambda_b = \ln 2/t_{\frac{1}{2}}$; where $t_{\frac{1}{2}}$ = effective half-life of the second component of whole-body loss.

On the basis of this simple model, the absorbed dose in microscopic disease is dependent on tumour size by virtue of the inclusion of the ϕ factor in Equation (2). For bulk disease, $\phi = 1$ and, for constant uptake per unit mass, the absorbed dose is independent of tumour size. The possible injected activities were calculated to produce a whole-body dose of 2 Gy (taken to represent bone marrow tolerance) using the appropriate whole-body S factor. Tumour doses were calculated as a function of diameter, for a range of values of the effective mIBG half-time in tumour.

Sources of data

Moyes et al (1989) have recently reported the quantitative uptake of ^{125}I-mIBG in human neuroblastoma. Six children (five Stage IV, one Stage III) undergoing routine resection of their tumours were injected with low activities of ^{125}I-mIBG approximately 36 h prior to surgery. Following excision, surgical specimens were cut into small pieces and radioactivity measured by a well counter. Uptake data for the six patients are shown in Table I.

Data on the kinetic clearance of mIBG from the whole body were reported by Lashford et al (1988). Briefly, this study found that mIBG clearance was bi-exponential with the first component being very rapid and contributing little to whole-body dose. On average the second component of the decay had a biological half-time of 34 h and extrapolated back to 58% of the initial activity at the time of administration. Whole-body S factors for the whole-body masses shown in Table I were derived from NCRP report 73 (1983).

Absorbed fractions of beta-energy from the disintegration of ^{131}I for spherical volumes of various diameters have been reported (Humm, 1986). A more comprehensive set of data were kindly provided by Dr John Humm (written communication, 1988) and these are used in the calculations. For the dose–cure analysis, the clonogenic fraction was taken as 0.1, the cellular packing factor as 0.5 and the diameter of a tumour cell as 0.0124 mm (corresponding to a cellular volume of 1000 μm^3). These quantities are required to relate tumour volume to clonogenic cell number. The particular values chosen are approximate estimates.

The radiation–survival curve for neuroblastoma cells is taken to be exponential with a D_0 of 1.0 Gy. Although

Table I. Tumour uptake data on six children with neuroblastoma (five Stage IV, one Stage III) injected with ^{125}I-mIBG approximately 36 h before routine surgical resection (from Moyes et al, 1989). The variable in the last column (mass × uptake) may be a useful prognostic indicator (see text).

Patient	Mass (kg)	Mean tumour uptake (% per gram)	Range of uptake within tumour (% per gram)	Mass × uptake
1	10	0.051	0.019–0.071	510
2	21	0.027	0.022–0.045	567
3	15	0.023	0.005–0.061	345
4	16	0.0096	0.0034–0.018	154
5	63	0.0053	0.0032–0.03	334
6	15	0.0041	0.0013–0.0048	61

this is undoubtedly a simplification, this value is consistent with the median D_0 of published *in vitro* data as reviewed by Wheldon et al (1986). No repopulation factor for neuroblastoma cells was included in the present model.

Results

Dose–cure analysis

For any given set of choices for the parameters of Equation (1) the probability of cure is a sharply rising function of dose and follows an approximately sigmoid shape. Figure 1 shows the probability of cure for three different tumour diameters (0.2 mm, 1 mm and 10 mm; all other parameters kept constant) as a function of absorbed dose. For the purposes of this paper a cure probability of 50% was taken as a reference value for comparison with the calculated absorbed doses to tumours; however, the conclusions are not significantly affected if some other value, between about 20% and 80%, is chosen instead.

Absorbed dose in tumours

The calculated absorbed doses to tumours and the doses required for a cure probability of 50% for each of the six patients are shown, for an effective mIBG half-life in tumour of 60 h, in Fig. 2. The average whole-body dose in all these cases is 2 Gy. It can be seen that the tumour dose is dependent on the effective ^{131}I half-life in the tumour and on the tumour size. For tumour sizes greater than 2 cm diameter there is no longer any size effect and the calculated doses become those for electronic equilibrium (*i.e.* all disintegration energy is absorbed). The most important factor causing variations in absorbed dose between patients is the bound activity per unit mass of tumour. There is a good correlation between this quantity and the product of patient mass and proportional tumour uptake per unit mass. Figure 3 shows the calculated equilibrium tumour doses as a function of the product of mass × uptake for three different values of effective radionuclide half-life in tumour. There is a linear relationship between

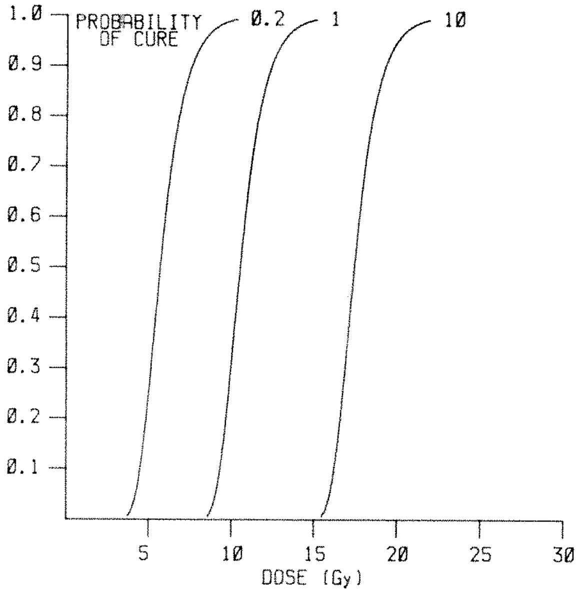

Figure 1. Variation in the probability of tumour cure by ^{131}I-mIBG as a function of dose for three different diameters of tumour: 0.2 mm, 1 mm and 10 mm. Cure probabilities were calculated as decribed in the text. For the purposes of calculation it was assumed that the clonogenic fraction was 0.1, the cellular packing factor was 0.5 and the diameter of a tumour cell was 0.0124 mm (corresponding to a cellular volume of 1000 μm^3).

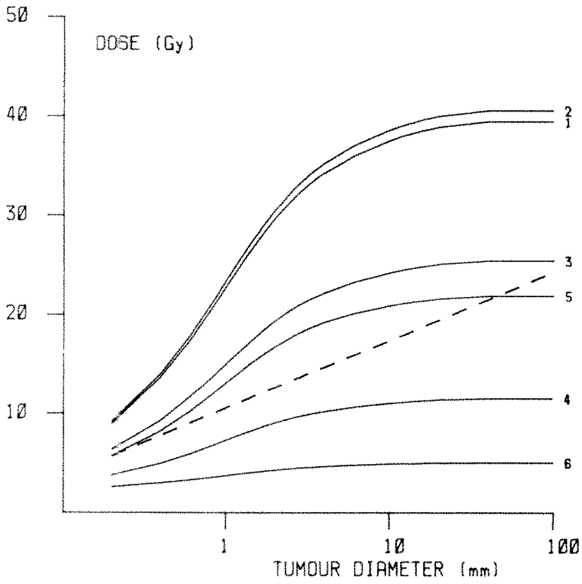

Figure 2. Calculated doses from single-agent ^{131}I-mIBG to neuroblastoma tumours with diameters from 0.2 mm to 100 mm for each of the six patients in the study for an effective ^{131}I half-life of 60 h. Patients are identified by the index numbers on the curves. The dashed line represents the doses which are calculated to give a cure probability of 50% based on the analysis in the text.

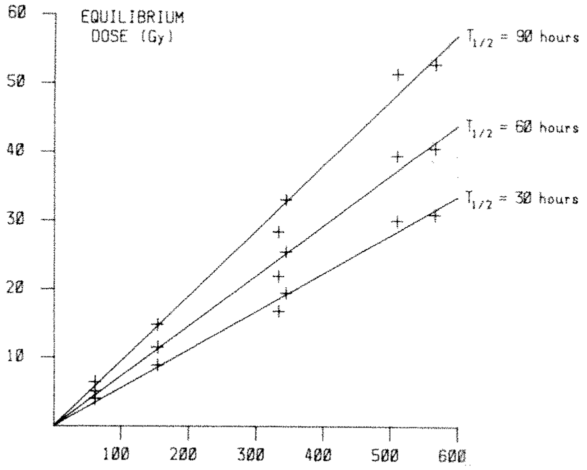

Figure 3. Calculated values of the equilibrium tumour dose as a function of the product of patient mass and proportional uptake per unit mass of tumour for three different values of the effective tumour half-life of mIBG: 30, 60 and 90 h. The equilibrium dose is the absorbed dose for conditions where all the radionuclide disintegration energy is absorbed in the tumour. There is a linear relationship (correlation coefficients >0.99) and it is suggested that this product may be a clinically useful prognostic variable (see text).

Table II. Effective tumour half-lives of 30 h and 90 h

Tumour diameter (mm)	Patient					
	1	2	3	4	5	6
0.2	c;c	c;c	f;c	f;f	f;c	f;f
1.0	c;c	c;c	c;c	f;f	f;c	f;f
10.0	c;c	c;c	f;c	f;f	f;c	f;f

Prognostic categories for the six patients of the study as described in the text. The first letter refers to the therapeutic outcome for an effective tumour half-life of 30 h, the second for 90 h. c, denotes calculated dose greater than dose for 50% probability of cure; f, denotes calculated dose less than dose for 50% probability of cure.

equilibrium dose and mass × uptake (correlation coefficients >0.99). Table I includes the values of mass × uptake for the study patients.

For non-equilibrium conditions, Fig. 2 indicates that the likelihood of achieving cure depends on the size of tumour. On this model, which assumes uniform uptake throughout the tumour, the smallest diameter tumours are more difficult to cure than those with diameters in the 1–10 mm range. This is because the reduction in the number of tumour cells in smaller tumours is offset by the decrease in energy absorption. The likelihood of tumour cure improves as the effective radionuclide half-life in the tumour (*i.e.* the retention) increases. Additionally, as the tumour retention increases, the minimum size of tumour that can be cured becomes less. These findings can be expressed by forming two prognostic categories: cure (c)—the predicted dose is greater than or equal to the 50% cure dose, and fail (f)—the predicted dose is less than the 50% cure dose.

For any particular tumour size, the category into which a patient falls depends on the uptake and retention of mIBG by the tumour. Table II shows the results for each patient in the study for tumour diameters of 0.2, 1 and 10 mm with effective radionuclide half-lives of 30 h and 90 h. For a half-life of 30 h, tumours of all sizes in the range of 0.2–10 mm diameter are predicted to be curable in only two of the six patients (Patients 1 and 2). These are the patients with the highest values of mass × uptake (see Table I). An effective radionuclide half-life of 30 h corresponds to no enhanced retention of mIBG in tumour compared with the biological clearance from the rest of the body. For a half-life of 90 h tumours of all sizes in the range of 0.2–10 mm diameter are predicted to be curable in four of the six patients (Patients 1 and 2, as before, and also Patients 3 and 5). The latter two patients have intermediate values of mass × uptake. No cures are predicted for Patients 4 and 6 for any size of tumour.

Discussion

The patients discussed here did not progress to mIBG therapy and so comparison of predicted with actual outcome is inappropriate. Nevertheless, the findings may be helpful in identifying the potential problem areas of this sort of treatment and to form a conceptual framework so that subsequent clinical findings may be more readily understood.

Tumour doses are critically dependent on cumulated activity per gram of tumour. This quantity is determined by the level of uptake of radionuclide and the subsequent activity–time profile. Uptake, in terms of activity per gram, is simply the product of the amount of activity that is initially administered and the proportional uptake per gram of tumour. The activity that can be administered, within the constraints imposed by the tolerance of the haemopoietic system, to any particular patient depends on the mass of that patient. The greater the patient mass the higher the activity that can be given for similar clearance kinetics. Tumour dose is therefore directly related to patient mass. For two patients with the same proportional uptake per gram of tumour, the more massive patient will receive a greater tumour dose simply because a higher activity can be administered. This is of particular importance for paediatric patients where the range of body weights can be wide. It also means that the product of the patient mass and the percentage uptake (per unit mass of tumour) may be a useful prognostic indicator in cases where the latter quantity can be estimated. Ideally, one would wish to measure tumour uptake by pre-surgical administration of tracer amounts of ^{125}I-mIBG as described by Moyes et al (1989). If this is not possible then tumour uptake could be estimated by scintigraphic imaging in conjunction with tumour volume estimation using computed tomographic (CT) or ultrasound examination. For the data examined in this paper, values of mass × uptake less than about 200 seem to suggest a poor prognosis, meaning that few or no tumours of any size will be cured even for favourable tumour retention of mIBG.

The likelihood of cure is increased for enhanced tumour retention (see Table II). This suggests that if there was a way of increasing the tumour retention, an increased level of cure or long-term remission could be achieved. In this regard, the calcium channel blocking the drug nifedipine has been reported to increase tumour retention of mIBG in phaeochromocytoma (Blake et al, 1988). Even with the maximum effective half-life considered, it can be seen that for two patients (4 and 6) no tumours of any size would be predicted to be cured. Single-agent ^{131}I-mIBG does not seem to be a curative therapeutic strategy for these patients. The analysis suggests there may be a worthwhile therapeutic effect for the other patients but, even for the highest tumour uptakes, there may be difficulties in curing microtumours of the order of 200 μm in diameter. In reality, the problems associated with these sizes are likely to be greater still as a multiplicity of micrometastases would be anticipated to be present. This gives rise to the possibility that, for patients with high tumour uptakes, therapy may fail owing to the regeneration or growth through treatment of "clumps" of tumour cells that were of undetectably small size at the initiation of therapy. Clinically, this may be manifested as the sudden appearance of a number of previously unobserved fast-growing metastases some time after therapy. This suggests the need for an element of therapy that would be appropriate for very small "clumps" and individual tumour cells. This element could have either of two forms:

(1) A non-specific but pervasive cytotoxic agent, *i.e.* systemic chemotherapy or total-body irradiation (TBI).
(2) Highly localized biologically targeted therapy *e.g.* a short-range radionuclide or an immunotoxin.

Of these alternatives the former would appear to be the most easily implemented at the present time.

In these calculations the model for absorbed dose to tumours was used with the measurements described in the Sources of Data section. This suffers from the disadvantage that the tumour uptakes and pharmacokinetic data are not patient-matched. Clinically, one would anticipate matched data that would take more fully into account variations in both tumour uptake and retention and also pharmacokinetic parameters for individual patients.

The results are, of course, subject to the set of assumptions upon which the model is based. The most important sources of error are likely to be the neglect of intratumour heterogeneity of uptake and the assumption that the uptakes measured following surgical excision of bulk tumours are applicable to micrometastases. Table I indicates that there is a substantial variation in the measured uptake of ^{125}I-mIBG throughout the excised tumours. The existence of intratumour heterogeneity will cause regions of relatively high and low dose. Tumour regeneration could proceed from unsterilized cells in low-dose regions. This phenomenon is likely to be more important in larger tumours (where diffusion of mIBG may be less uniform). As a result of the neglect of heterogeneity, the calculated cure probabilities are likely to be optimistic for macroscopic tumours.

Other sources of error in the analysis are due to tumour radiobiology. An exponential radiation survival curve with a D_0 of 1 Gy was assumed. This is consistent with the median parameters found for a group of eight human neuroblastoma cell lines grown *in vitro* as either monolayer cultures or as multicellular tumour spheroids (Wheldon et al, 1986). However, there was a significant degree of variability in the parameter D_0 in this group (range 2.26–0.66 Gy). Additionally, some survival curves were not pure exponentials but had a pronounced "shoulder", *i.e.* a region of relatively reduced radiosensitivity at small doses. It is anticipated that variability in radiosensitivity will not correlate with mIBG uptake and therefore that it will not affect the general conclusions of this study, although it could be an important factor for any particular patient.

A source of error that could possibly be important is tumour kinetics. Little is known about the proliferation of tumour cells and their cell cycle redistribution over a course of irradiation by a decreasing dose-rate. However it is possible that there will be an inhibition of cell cycle progression (and hence no proliferation) if the dose-rate is high enough. As the dose-rate decreases this inhibition may be removed and progression may begin. If this is true there will be two effects of importance. The first of these is that cellular repopulation in tumours with lower uptakes will begin earlier. The second is that repopulation will begin earlier in smaller tumours than larger ones because the dose-rate is less (due to reduced absorption). This will mean that tumours with low uptakes and those of smaller size will be even more difficult to sterilize than suggested in the analysis. Finally, the clonogenic fraction of tumour cells was taken to be 0.1 for all sizes of tumour. The dose for a cure probability of 50% is quite insensitive to this factor. (For a clonogenic fraction of 1.0 the cure doses are increased by 2.3 Gy, while for a clonogenic fraction of 0.01 they are reduced by 2.3 Gy.) It seems reasonable that the clonogenic fraction will be higher in smaller tumours than larger ones, since the clonogenic fraction must be exactly 1 at the single-cell level.

In summary, most of the possible sources of error in this analysis, although not directly quantifiable at present, will have the effect of increasing the difficulty of sterilizing tumours that have already poor prognoses, especially those of smaller sizes. The present analysis gives an indication of cure probabilities in favourable circumstances, and provides a measure of the improvements that may be necessary to obtain high cure probabilities in more realistic situations. Finally, although we have been discussing treatment with mIBG in this paper, the findings would be equally applicable to targeted ^{131}I radiotherapy with other molecular delivery vehicles including antibodies.

Conclusions

A method has been developed to estimate the predicted absorbed doses to tumours from ^{131}I-mIBG therapy and the associated probabilities of tumour cure. Based on measurements of ^{125}I-mIBG uptake in surgically excised neuroblastomas for six patients, the predicted doses to tumours of varying size were calculated. It is suggested that the product of patient mass and measured percentage uptake per gram of tumour may be a good indicator of therapeutic outcome. The probabilities of cure are higher for enhanced tumour retention of mIBG. Tumours of 200 μm diameter appear to be a particularly difficult size to cure and may necessitate the use of an additional appropriate therapeutic technique.

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Appendix 1

Let there be N_0 tumour cells, of which a proportion, k, are clonogenic, *i.e.* there are kN_0 clonogenic cells present initially. Following radiation, if a fraction S of these clonogenic cells survive, the mean number of clonogenic cells remaining will be SkN_0. This would be the mean number for a statistical population of tumours. For any one tumour, the probability of zero surviving cells is given by the first term of a Poisson series with mean SkN_0. We assume that tumour recurrence will follow if even one clonogen survives, hence the probability of cure (P_c) is the same as the probability of zero surviving cells, viz.

$$P_c = \exp(-SkN_0) \qquad (1.1)$$

The surviving fraction of tumour cells following a dose D_P is given by:

$$S = \exp(-D_P/D_0) \qquad (1.2)$$

where D_0 represents the radiosensitivity of the tumour cells.

N_0, the initial number of tumour cells, is given by:

$$N_0 = (d_t/d_c)^3 f \qquad (1.3)$$

where d_t = diameter of tumour; d_c = average diameter of a tumour cell and f = a cellular packing factor, *i.e.* the proportion of the tumour volume consisting of tumour cells.

It follows from Equations 1.1, 1.2 and 1.3 that:

$$D_P = D_0 \ln\{kf(d_t/d_c)^3/\ln(1/P_c)\} \qquad (1.4)$$

This is Equation (1) in the text.

Appendix 2

The absorbed dose, D_T, to a tumour is composed of three components.

$$D_T = D^{\beta}_{\text{bound}} + D^{\beta}_{\text{non-bound}} + D^{\gamma}_{\text{non-bound}} \qquad (2.1)$$

where D^{β}_{bound} is the dose from the β-emissions of activity bound to tumour, $D^{\beta}_{\text{non-bound}}$ is the dose from the β-emissions of activity in the body but not bound to the tumour (negligible in the case of bulk tumour) and $D^{\gamma}_{\text{non-bound}}$ is the dose from the γ-emissions of activity in the body. The dose to tumour from γ-emissions of activity bound to the tumour is assumed to be negligible.

β dose-rate from bound activity

The dose-rate from this component is given by:

$$R^{\beta}_{\text{bound}}(t) = T(t)\phi D_{\beta} \qquad (2.2)$$

where $T(t)$ = activity per gram of tumour; ϕ = absorbed fraction of β-energy for tumour; and D_{β} = equilibrium β-dose constant for ^{131}I.

$$T(t) = A_0 u_0 \exp(-t\ln 2/T_{\frac{1}{2}}) \qquad (2.3)$$

where A_0 = total injected activity and u_0 = initial proportional uptake per gram of tumour (= $u\exp(T_{\text{gap}}\ln 2/T_{\text{biol}})$; where u = the measured proportional uptake per gram of tumour at a time, T_{gap} following injection of ^{125}I-mIBG. T_{biol} = biological half-life of ^{125}I in the tumour and $T_{\frac{1}{2}}$ = effective half-life of ^{131}I-mIBG in the tumour = $(T_{\text{phys}} T_{\text{biol}})/(T_{\text{phys}} + T_{\text{biol}})$ where T_{phys} = physical half-life of ^{131}I.

β dose-rate from unbound activity

The whole-body clearance kinetics are assumed to be bi-exponential with the first component being very fast and contributing little to dose (Lashford et al, 1988). Only the second component will be responsible for dose to tumours and the whole body. The dose-rate from this component is given by:

$$R^{\beta}_{\text{non-bound}}(t) = B(t)(1-\phi)D_{\beta} \qquad (2.4)$$

where $B(t)$ = activity per gram in the whole body.

$$B(t) = FA_0/m \exp(-t\ln 2/t_{\frac{1}{2}}) \qquad (2.5)$$

where F = proportion of the initial activity lost from the whole body with an effective half-life corresponding to the second component of the bi-exponential decay; $t_{\frac{1}{2}}$ = effective half-life of the second component of whole-body loss; m = patient weight in grams.

γ dose-rate from unbound activity

The dose rate from this component is given by:

$$R^{\gamma}_{\text{non-bound}}(t) = B(t)D_{\gamma} \qquad (2.6)$$

where D_{γ} = effective γ dose constant for ^{131}I. D_{γ} may be estimated by:

$$D_{\gamma} = mS_{\text{WB-WB}} - D_{\beta} \qquad (2.7)$$

where $S_{\text{WB-WB}}$ = whole-body to whole-body absorbed dose per unit cumulated activity for ^{131}I (in Gy/MBq h).

This follows since the product mS_{WB-WB} is the effective dose constant for all emissions for a patient of mass m.

Total dose-rate

From Equation 2.1 this is the sum of the three components given by equations 2.2, 2.4 and 2.6:

$$R_T(t) = T(t)\phi D_\beta + B(t)(1-\phi)D_\beta + B(t)D_\gamma \qquad (2.8)$$

which, using equations 2.3, 2.5 and 2.7 can be reduced to:

$$R_T(t) = k_t \exp(-\lambda_t t) + k_b \exp(-\lambda_b t) \qquad (2.9)$$

where $k_t = A_0 u_0 \phi D_\beta$; $k_b = A_0 F/m(mS_{WB-WB} - \phi D_\beta)$; $\lambda_t = \ln 2/T_{\frac{1}{2}}$ and $\lambda_b = \ln 2/t_{\frac{1}{2}}$.

The total dose:

$$D_T = \int_0^\infty R_T(t)\,dt = k_t/\lambda_t + k_b/\lambda_b \qquad (2.10)$$

which is Equation (3) in the text.

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Haemodynamic effects of water-soluble contrast media on the isolated perfused rat kidney

By *A. A. El Sayed, MB, BCh, *J. L. Haylor, BPharm, PhD, †A. M. El Nahas, FRCP, PhD, ‡S. Salzano, BSc, MSc and §S. K. Morcos, FRCS, FFRRCSI, FRCR

*Department of Medicine and Pharmacology, University of Sheffield, ‡Operational Research Unit, Trent Regional Health Authority and Departments of †Renal Medicine and §Radiodiagnosis, Northern General Hospital, Sheffield, UK

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Keywords: Contrast media, Isolated perfused rat kidney, Renal vascular resistance, Osmolarity

Abstract. The precise mechanism underlying the nephrotoxicity of radiocontrast media remains ill defined. In this study we have examined the direct effect of a wide range of low- and high-osmolar water-soluble contrast media (WSCM) on the vascular resistance of the isolated perfused rat kidney (IPRK). Water-soluble contrast media led to a significant fall in the renal perfusate flow and an increase in the renal vascular resistance (RVR). The magnitude of these haemodynamic changes was independent of the osmolality of the tested agents. This study shows a direct effect of WSCM on the vascular resistance of the isolated perfused rat kidney.

The importance of water-soluble contrast media (WSCM) nephrotoxicity in clinical practice has recently been the subject of renewed interest (Brezis & Epstein, 1989; Parfrey et al, 1989; Schwab et al, 1989; Dawson & Trewhella, 1990; Russo et al, 1990). Conflicting data are emerging relating to the incidence and clinical relevance of such nephrotoxicity (Katzberg, 1989). Whilst data from the United Kingdom suggests a low incidence of renal functional impairment, reports from the United States have shown an increasing incidence of nephrotoxicity, in particular in patients with underlying renal diseases (Byrd & Sheerman, 1979; Older, 1979; Webb et al, 1981). Until now, attempts to minimize the nephrotoxicity of WSCM have been hampered by our limited understanding of its pathophysiology.

In experimental animals the acute renal haemodynamic effect of contrast media is characterized by a biphasic response involving a transient decrease in vascular resistance followed by a more sustained increase (Russell & Sherwood, 1974; Vari et al, 1988; Haylor et al, 1990). A fall in glomerular filtration rate is also observed (Webb, 1984). The precise mechanism underlying radiocontrast-induced decrease in renal perfusion remains unknown. Some have suggested an indirect effect through a fall in cardiac output or a peripheral vasodilatation (Higgins, 1980; Dawson & Edgerton, 1983); others have postulated a direct effect on renal vasculature (Katzberg et al, 1982). The mediators of these changes are also poorly defined. A role for systemic hormones and renal autocoids has been put forward. These include antidiuretic hormone (ADH) (Trewhella et al, 1990), atriopeptins (Bentley et al, 1989), angiotensin II, thromboxane (Katzberg et al, 1982) and adenosine (Arend et al, 1987; Deray et al, 1989). Increase in the intrarenal interstitial pressure has also been implicated (Katzberg et al, 1982).

As *in vivo* studies have so far failed to dissociate the systemic from the direct effects of contrast media on the kidney, we have designed a new experimental approach based on the isolated perfused rat kidney (IPRK). In this study we have examined the direct effects of a wide range of WSCM, including high- and low-osmolar media, on the vascular resistance of the IPRK.

Materials and methods

Isolated perfused rat kidney preparation (Fig. 1)

Kidneys from adult male Wistar rats weighing approximately 400 g were used throughout the study. Rats were anaesthetized by an intraperitoneal injection of sodium pentobarbital (60 mg/kg, i.p.) and placed on a heated dissection table. After mid-line laparotomy the right ureter was cannulated. An intravenous bolus injection of heparin (500 units/kg) was administered into the femoral vein. The superior mesenteric artery was cannulated and the cannula advanced across the aorta into the right renal artery. The right kidney was perfused, *in situ*, with Krebs-Henseleit solution until blanching. The kidney was then removed and perfused at a constant pressure (100 mmHg) in a recirculating system with a perfusate (150 ml) based on a Krebs-Henseleit solution containing bovine serum albumin (6.7%) and mixed amino acids, Synthamin 14 (Travenol) (2 mmol). The perfusate was gassed with 95% oxygen and 5% CO_2 and warmed to 37°C. Pressure at the tip of the cannula was maintained at 100 mmHg by a servo-controlled peristaltic pump (Watson-Marlow 503) and the perfusion pressure was constantly monitored from a 27G needle placed inside the renal artery cannula. Perfusate flow

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Address correspondence to: Dr S. K. Morcos, Department of Diagnostic Imaging, Northern General Hospital, Herries Road, Sheffield S5 7AU, UK.

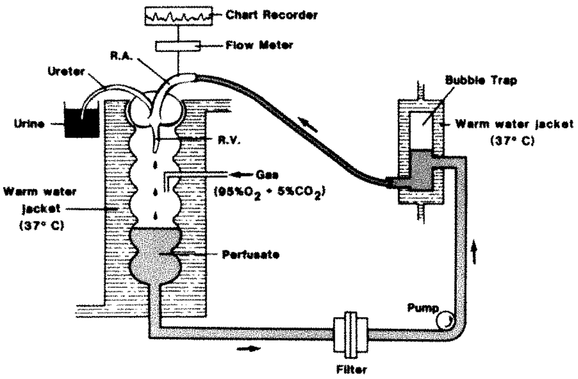
Chart Recorder
Flow Meter
R.A.
Ureter
Urine
Bubble Trap
Warm water jacket (37° C)
R.V.
Gas ($95\%O_2 + 5\%CO_2$)
Warm water jacket (37° C)
Perfusate
Pump
Filter

Figure 1. Schematic diagram for the IPRK, "the closed circuit model". The pump maintained the renal perfusion at a constant pressure of 100 mmHg. Arrows indicate the flow direction of the perfusate into the renal artery (RA). The venous return was collected in the perfusate reservoir via the renal vein (RV). The contrast medium (10 ml) was added directly to the perfusate in the reservoir.

was monitored using both an in-line flowmeter and from the continuous recording of pump speed. The techniques were based on the methodology of the isolated perfused rat kidney we have recently described (El-Sayed et al, 1990), which involved some modifications of those described by Maack (1986).

Experimental protocol and parameters

The experimental protocol was designed to assess the effect of high- and low-osmolar WSCM on the IPRK. After cannulation of the kidney and its isolation, each kidney was perfused for an equilibration period of 30 min. This was followed by a 10 min baseline period (30–40 min). At the end of this period, WSCM (10 ml) was added to the perfusate reservoir. This dose is comparable to the maximum tolerated intravenous dose of WSCM (8 ml/kg body weight) used in *in vivo* studies in rats (Reed et al, 1983). The dose was calculated on the assumption of a circulating blood volume in rats of between 15 and 20 ml perfusing two native kidneys, whilst in the IPRK model one kidney is perfused with 150 ml. At the final 10 min experimental period (40–50 min) the effect of the WSCM on renal perfusate flow (RPF) was examined. Groups of four kidneys were studied for control and experimental groups.

The WSCM studied included the high-osmolar contrast agents (HOCA): sodium iothalamate 420 mgI/ml, 2500 mosmol/kgH_2O (May & Baker), sodium iodamide 300 mgI/ml, 1592 mosmol/kgH_2O (Merck), and sodium-meglumine diatrizoate 325 mgI/ml, 1650 mosmol/kgH_2O (Schering AG). The low-osmolar contrast agents (LOCA) included: sodium-meglumine-ioxaglate 320 mgI/ml, 580 mosmol/kgH_2O (May & Baker), iopromide 370 mgI/ml, 780 mosmol/kgH_2O (Schering AG), iohexol 350 mgI/ml, 880 mosmol/kgH_2O (Nycomed), and iopamidol 340 mgI/ml, 681 mosmol/kgH_2O (Merck).

Comparisons were made within individual kidneys before (baseline period) and after (experimental period) the injection of WSCM. Comparisons were also made between the experimental period of injected kidneys and the untreated controls (40–50 min).

Statistical analysis of the data

Results are expressed as mean ± standard error of the mean (M ± SEM). Within-group comparisons were analysed by the paired *t*-test. In-between groups comparisons were analysed by one-way analysis of variance (ANOVA) or analysis of covariance (ANCOVA) as appropriate. The p value of < 0.05 was considered to be significant.

Results

In the control, untreated group, no significant change in RPF occurred throughout the observation time. The injection of WSCM led invariably to a significant reduction in RPF. However, the character of the renal haemodynamic response differed slightly between high- and low-osmolar agents (Fig. 2). Following the injection of high-osmolar agents a transient increase in RPF preceded the sharp and sustained decrease. By contrast the injection of LOCA led to an immediate transient marked decrease in RPF followed by a sustained but a milder decrease in the perfusate flow (Fig. 2). The magnitude of the fall in RPF and, consequently, the increase in renal vascular resistance (RVR) was proportional to the baseline flow rate; regression coefficient (r) was -0.476, $p < 0.0005$ (Fig. 3). When the results were adjusted for the baseline variations, the decrease in RPF produced by WSCM remained significant within the groups (Table I) as well as in comparison to the untreated control groups (Table II).

Overall, no significant difference ($p = 0.278$) was found for the extent of increase in RVR induced by HOCA and LOCA. The mean change in RPF with HOCA ($n = 12$) was -14.23 ml/min and with LOCA ($n = 16$) was -11.4 ml/min. Furthermore, no correlation was observed between the osmolarity of the tested agents and the amount of reduction induced by them in RPF, $r = 0.12$, $p > 0.05$ (Fig. 4). The smallest reduction

Table I. Amount of change in RPF (the difference between the value of RPF at the end of the baseline period and at the end of the experimental period) in the different groups adjusted for baseline variations

Mean ± SEM of the amount of change in RPF (ml/min)		
Control	-2.50 ± 1.49	$p = 0.106$
Sodium iothalamate 420	-14.05 ± 1.96	$p < 0.0005$
Sodium iodamide 300	-12.87 ± 1.74	$p < 0.0005$
Diatrizoate 325	-8.94 ± 1.73	$p < 0.0005$
Iohexol 350	-14.17 ± 1.92	$p < 0.0005$
Iopamidol 340	-12.37 ± 1.93	$p < 0.0005$
Ioxaglate 320	-12.27 ± 1.91	$p < 0.0005$
Iopromide 370	-9.25 ± 1.80	$p < 0.0005$

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Intersite comparison of the Hologic QDR-1000 dual energy X-ray bone densitometer

By *G. M. Blake, PhD, †C. M. Tong, MSc, and *I. Fogelman, MD, FRCP

*Department of Nuclear Medicine, Guy's Hospital, St Thomas Street, London, SE1 9RT, UK and
†Department of Nuclear Medicine, Queen Mary Hospital, Hong Kong

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Keywords: X-ray dual photon absorptiometry, Bone mineral density

Abstract. We have compared results from 13 Hologic QDR-1000 bone densitometers: (i) by performing spine and hip scans on two normal volunteers; (ii) by acquiring sets of 10 sequential scans on a Hologic anthropomorphic spine phantom. For each QDR-1000 site visited a set of spine phantom scans was also acquired on a QDR-1000 at Guy's Hospital to serve as a control study. All scans were analysed using the Hologic scan comparison software. Radiographers at each site were asked to perform their own independent analysis of the scans of the two volunteers. The precision of the bone mineral density (BMD), bone mineral content (BMC) and projected area (Area) results for a set of 10 phantom scans was 0.11%, 0.14% and 0.12% respectively. The coefficient of variation (CV) between sites for the sets of phantom scans was 0.58% for BMD, 0.71% for BMC and 0.35% for Area. In comparison, CVs for the phantom scans acquired on a single QDR-1000 were 0.23%, 0.23% and 0.09% respectively. The CV for the BMD results on the two volunteers obtained using the scan comparison software averaged 1.4% for the spine and 2.1% for the femoral neck. The CV for the results obtained by site radiographers averaged 2.2% for the spine and 3.7% for the femoral neck. Significant differences in the technique used for hip analysis were found. Conclusions: (i) differences in calibration between systems were generally less than 1%; (ii) variations in results resulting from differences in analytical technique were more significant than those resulting from differences in calibration.

1. Introduction

Osteoporosis is widely recognized as a major cause of morbidity and mortality amongst elderly women, with important financial implications for the provisions of health care and social services (Bengner et al, 1988; Royal College of Physicians Report, 1989). Although little can be done to reverse established osteoporosis, there are strong reasons to believe that screening women at the menopause to select patients for prophylactic therapy may significantly reduce the incidence of osteoporotic fractures in later life (Fogelman et al, 1990). Coupled with this clinical interest in osteoporosis, there has been a significant growth of interest in the application of non-invasive physical methods for measuring bone mass (Tothill, 1989). Amongst these, absorptiometry has become established as a convenient and precise method of measurement (Fogelman et al, 1990). Single photon absorptiometry has been used to measure bone mass in the forearm (Cameron & Sorenson, 1963; Mazess et al, 1984), while dual photon absorptiometry (DPA) permits measurements at the clinically important sites of the spine and femoral neck (Wilson & Madsen, 1977; Rodin et al, 1990). Until recently, most DPA systems utilized a high activity sealed radioactive source of ^{153}Gd, a nuclide whose discrete photon emissions at 44 keV and 100 keV are ideal for absorptiometry (Tothill, 1989). Over the past 2 years, however, dual energy X-ray absorptiometry (DEXA) has superseded DPA (Kelly et al, 1988; Pacifici et al, 1988; Cullum et al, 1989; Mazess et al, 1989). The higher photon flux from DEXA scanners results in higher spatial resolution, improved precision, shorter scanning times and reduced radiation dose to the patient. A further significant advantage of DEXA scanners is that they can be accurately calibrated in the factory before installation in the clinical environment. In the absence of radioactive decay and the consequent need for frequent replacement of a radioactive source, a DEXA scanner should maintain its calibration with high precision during clinical use. Thus DEXA scanners in different clinical institutions should maintain good agreement between themselves. In this report, we describe a study of the intersite variations in calibration of one type of DEXA scanner, the Hologic QDR-1000. We have performed phantom studies together with spine and hip scans on two normal volunteers on 13 QDR-1000 systems to compare their phantom and *in vivo* calibration.

2. Materials and methods

2.1 *The Hologic QDR-1000*

The QDR-1000 (Cullum et al, 1989) produces continuous X-ray spectra at two different effective photon energies by switching its HV generator between 70 kV_p and 140 kV_p during alternate half-cycles of the mains supply. As it scans the patient, the pencil X-ray beam is passed through a rapidly spinning reference wheel divided into three sectors. These consist of: (i) a sector containing an open air gap; (ii) a sector containing a soft tissue equivalent medium; (iii) a sector containing a bone equivalent medium. Measurements through the air sector give the attenuation through the patient's body, while measurements through the bone and soft tissue sectors measure the incremental attenuation due to known amounts of bone and soft tissue. The reference wheel serves as an internal standard against which the bone mass in any scan image is assessed. Each QDR-1000 is supplied with an anthropomorphic spine phantom that serves as a test object: daily scans of this phantom are made and the measured values of bone mineral content (BMC), projected area (Area) and bone mineral density (BMD = BMC/Area) are recorded on a database. Inspection for any trends in these daily measurements enables the consistency of calibration to be checked. At the time of manufacture, each system is calibrated against a master phantom that contains samples of bone equivalent medium with BMD values of approximately 0.6, 1.0 and 1.6 g/cm^2. After calibration, the QDR-1000 is assigned an anthropomorphic spine phantom, and the BMC value of the latter is measured using the newly calibrated scanner. Any subsequent variation in calibration can be detected by reference to this site phantom.

2.2 Study protocol

The following study protocol was performed for each of 13 different QDR-1000 systems located at 12 sites throughout the UK.

(1) The study was commenced with five sequential scans on the site spine phantom. Use was made of the "autoscan" facility wich permits repeated scanning of an object a predefined number of times without further operator intervention.

(2) Scans of the lumbar spine (L1–L4) and left hip were performed on two normal male volunteers aged 33 and 42. For the hip scan the leg was positioned parallel to the edge of the couch with the foot turned inwards at an angle of 27° and firmly clamped to a foot rest.

(3) Ten sequential scans were performed on a Hologic spine phantom (Serial No. Q-176) belonging to Guy's Hospital.

(4) The study was completed with a further five scans on the site spine phantom. By dividing the 10 scans on the site phantom into two groups acquired at the beginning and the end of the study, any variation in calibration during the study could be detected. After completion of steps (1) to (4) all scans were archived and returned to our institution for analysis.

(5) The site database containing the results of the daily scans of the site spine phantom was examined and the mean BMD, BMC and Area noted together with their coefficient of variation.

(6) For each QDR-1000 site visited, a set of 10 scans of the Q-176 spine phantom was acquired on a QDR-1000 at Guy's Hospital. The object of this was to verify that any difference found between systems was greater than when comparable data were acquired on a single system. During the entire study, a total of 50 sets of 10 phantom scans were acquired.

2.3 Analysis of spine phantom scans

All spine phantom scans were analysed using the Hologic scan comparison software which enabled the same analysis box to be set up for every scan. For each data set of 10 sequential scans of a spine phantom, the mean BMD, BMC and Area were calculated together with their standard deviation and standard error of the mean (SEM). It was convenient to express the standard deviation in terms of the coefficient of variation (CV) defined as follows:

$$\mathrm{CV} = \frac{\text{standard deviation of data set}}{\text{mean of data set}} \times 100 \qquad (1)$$

Similarly, it was convenient to express the SEM by normalizing it to the mean in the same manner. During the evaluation of our results it was necessary to know the precision of the BMD, BMC and Area measurements derived from a single data set. This was estimated by calculating the root mean square SEM as follows:

$$\text{precision of single data set} = \frac{\left(\sum_{i=1}^{N} \mathrm{SEM}_i^2\right)^{1/2}}{N} \qquad (2)$$

where $N = 50$ was the total number of phantom data sets.

2.4 Analysis of scans on normal volunteers

All scans on volunteers were analysed using the Hologic scan comparison software. When spine images were analysed, areas of transverse process identified as bone by the analysis software were included provided they were attached to the vertebral body; ribs and unattached areas of transverse process were deleted. During analysis of hip scans, the coordinates defining the midline of the femoral neck, the femoral neck box and trochanteric regions were set to be identical on successive studies. However, an independent search for Ward's triangle was performed on each image. Radiographers at each site were asked to perform their own independent analysis of the scans on the two volunteers.

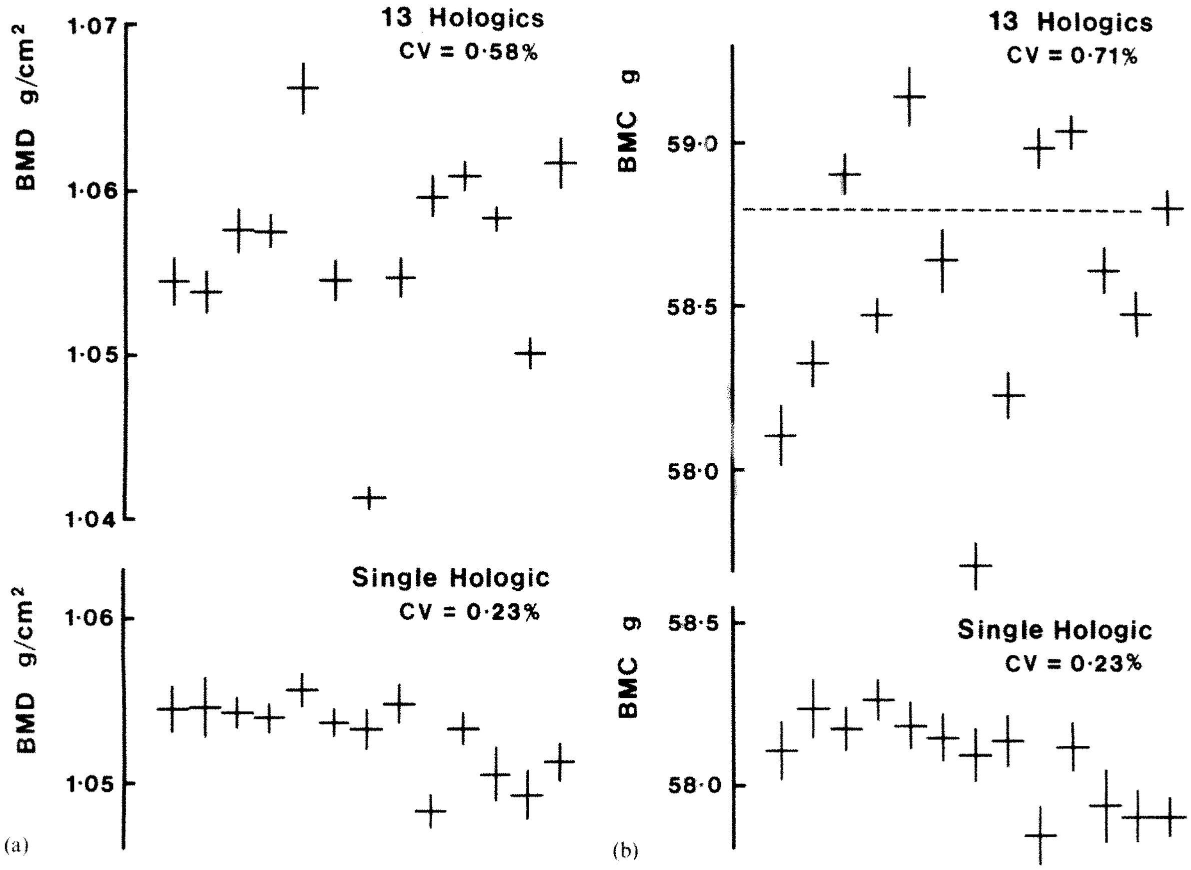
2.5 Statistical analysis

The *F*-distribution (Morrison, 1976) was used to compare variances and statistical significance assessed using the relevant degrees of freedom (df).

3 Results

3.1 Scans of spine phantom Q-176

3.1.1 Bone mineral density. The mean BMD results derived from scans of the Hologic phantom Q-176 acquired on 13 different QDR-1000 systems are plotted in Fig. 1(a). For comparison, the lower half of Fig. 1(a) shows the BMD results from 13 repeated studies of Q-176 acquired on a single system. Error bars show the individual SEMs calculated for each data set of 10 scans. When the SEMs were averaged over all the data sets (eqn (2)) the precision of a single set was 0.11% (df = 50). If no calibration differences exist between different systems then this precision is the expected value of the CV for the scan sets acquired at different



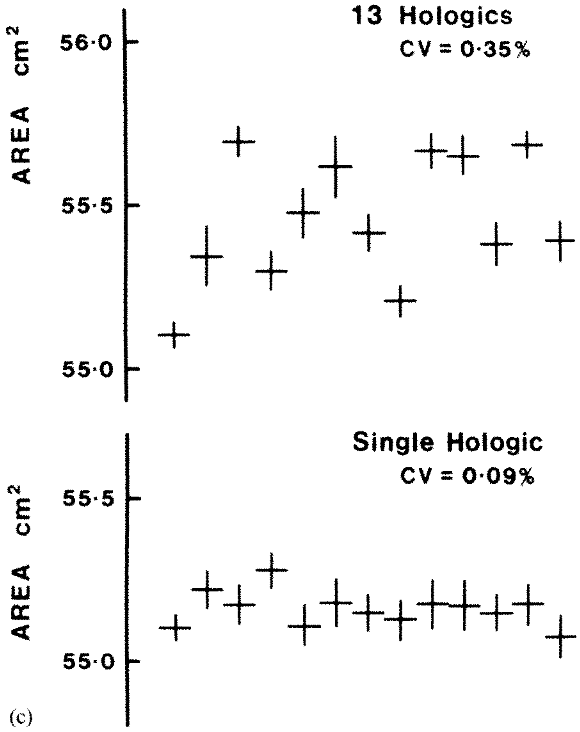


Figure 1. (a) Bone mineral density (BMD) results from scanning a single Hologic spine phantom on 13 different QDR-1000 systems (upper figure) compared with results of repeated studies on a single system (lower figure). Each BMD measurement plotted is the mean for a set of 10 sequential scans. Error bars show the standard error of mean for each scan set. (b) Bone mineral content (BMC) data for the spine phantom plotted in a manner comparable with the BMD data of Fig. 1(a). The broken line at 58.8 g shows the nominal factory calibration BMC for the Hologic phantom used. (c) Projected area data for the phantom plotted in a manner comparable with the BMD data of Fig. 1(a).

sites. Similarly, it is the expected CV for scan sets acquired on a single QDR-1000 provided no calibration changes occur. The CV for the BMD results for the 13 different systems was 0.58% (df = 12). Application of the F-test confirmed that significant differences exist between sites ($F = 27.8$, $p < 0.001$). The CV for studies acquired on a single system was 0.23% (df = 12), also significantly larger than expected ($F = 4.4$, $p < 0.001$). It is clear from Fig. 1(a) that a small shift in BMD calibration of the Guy's QDR-1000 occurred towards the end of the study.

3.1.2 Bone mineral content. Figure 1(b) shows BMC data for the Q-176 phantom plotted in a manner comparable with the BMD data of Fig. 1(a). The

Table I. Comparison of the results of site phantom scans acquired in this study with data recorded on each site phantom database

	BMD	BMC	Area
Root mean square (RMS) difference from site database (degrees of freedom = 13)	0.32%	0.41%	0.16%
Precision of set of 10 scans (degrees of freedom = 50)	0.11%	0.14%	0.12%
F-test comparison of RMS difference and study precision	$F=8.5$ $p<0.001$	$F=8.6$ $p<0.001$	$F=1.8$ NS

broken line in the upper half of the figure shows the nominal BMC for Q-176 (58.8 g) derived at factory calibration. The precision of a single set of 10 scans was 0.14% (eqn (2), df = 50). In comparison, the CV for different QDR-1000s was 0.71% (df = 12), confirming that significant differences exist between sites ($F = 25.7$, $p < 0.001$). The CV for studies on a single system (0.23%, df = 12) was also significantly larger than expected ($F = 2.7$, $p < 0.01$).

3.1.3 Projected area. Figure 1(c) shows Area data for the Q-176 phantom. The precision of a single scan set was 0.12% (eqn (2), df = 50). The CV for the different QDR-1000s (0.35%, df = 12) confirmed that significant differences exist between sites ($F = 8.5$, $p < 0.001$). For the studies on a single system the CV was 0.09% (df = 12, $F = 1.8$, NS).

3.2 Scans of site spine phantoms

3.2.1 Comparison of site phantom scans with site phantom database. The mean BMD, BMC and Area results derived from our set of 10 scans of each site phantom were compared with the mean values of these quantities recorded on the site phantom database. The objective was to check whether the calibration of each QDR-1000 on the day our measurements were made was representative of its performance since installation. The results, expressed as the root mean square difference between our study data and the site phantom database means, are given in Table I. Table I also summarizes the precision values for a set of 10 scans derived in Section 3.1, while in the final line the root mean square differences and measurement precisions are compared using the *F*-test. BMD and BMC differences were significantly greater than expected, but not those for Area.

3.2.2 Comparison of measured phantom BMCs with their Hologic calibration. As explained in Section 2.1, measurement of a site phantom BMC on a QDR-1000 should reveal any changes that have occurred in the latter since factory calibration. The differences (measured phantom BMC − factory calibration BMC) had a mean of −0.05 g and a standard deviation of 0.32 g (df = 13). The expected value for the standard deviation, if no variation in system calibration had occurred, was the study precision of 0.08 g (df = 50). Measured and expected standard deviations were significantly different ($F = 15.6$, $p < 0.001$).

3.2.3 Verification of site phantom BMCs. During this study each site phantom was scanned alongside the Q-176 phantom. Hence, independently of any variation in QDR-1000 calibration, we could measure each site phantom BMC by reference to the factory calibration for Q-176 (58.8 g):

Site phantom BMC normalized to Q-176 =

$$\frac{\text{Hologic analysis BMC for site phantom}}{\text{Hologic analysis BMC for Q-176}} \times 58.8\ \text{g} \quad (3)$$

Equation (3) assumes that the factory calibration of Q-176 was exactly correct, when actually it was subject to the same statistical measurement errors as the other site phantoms. A consistent set of phantom BMCs was therefore derived by rescaling the results of eqn (3) to ensure that the sum of all measured BMCs agreed with the sum of factory calibration values:

Rescaled site phantom BMC =

$$\text{Normalized phantom BMC from eqn (3)} \times \frac{\Sigma\ \text{Factory calibration values}}{\Sigma\ \text{Normalized phantom BMCs from eqn (3)}} \quad (4)$$

The precision of a site phantom BMC measurement calculated from eqn (4) was 0.11 g, compared with the nominal error of 0.2 g printed on the side of each phantom. The standard deviation of the differences between the phantom BMCs derived from eqn (4) and the factory calibration values was 0.29 g.

3.3 CVs recorded on site phantom databases

At each site visited, the CVs of the daily BMD, BMC and Area measurements of the site phantom recorded on the site database were noted together with the total number of entries. The BMD CVs from the smallest (0.33%) to the largest (0.62%) are plotted in Fig. 2. The error bars are 95% confidence intervals calculated for the number of entries on each database using the *F*-distribution. The root mean square CV for the BMD results on all sets of phantom scans acquired during our study was 0.36%: this value is plotted as the broken line across Fig. 2. Site CVs between 0.32% and 0.40% were statistically consistent with this figure.

3.4 Scans of normal volunteers

The mean BMDs and their CVs for the spine and left hip scans of the two volunteers are listed in Table II. The mean CV was 1.4% for the spine, 2.1% for the femoral neck, 1.8% for the trochanter and 3.2% for Ward's triangle. In comparison, the CVs expected for a set of measurements on a single system are around 1% for the spine (Cullum et al, 1989), 2% for the femoral neck, 1.5% for the trochanter and 3% for Ward's triangle (figures from manufacturer's literature on hip analysis).

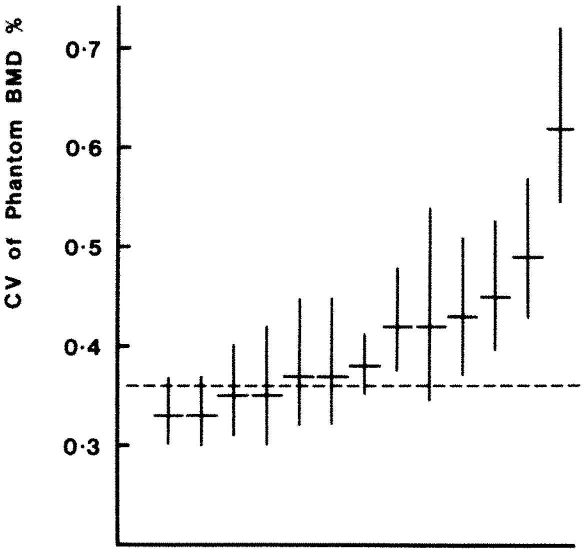


Figure 2. Coefficients of variation (CV) for the site phantom BMD results recorded on the site phantom database of 13 QDR-1000 systems. Data are plotted in order from smallest to largest CV. Error bars are 95% confidence intervals calculated from the number of entries on each database. The broken line at 0.36% is the root mean square CV derived from all the sets of phantom scans acquired during this study.

Table III. Mean BMDs and coefficients of variation (CV) for the spine and hip scans of two normal volunteers independently analysed by site radiographers

	Volunteer 1		Volunteer 2	
	Mean BMD (g/cm^2)	CV	Mean BMD (g/cm^2)	CV
Spine (L1–L4)	1.152	2.6%	1.161	1.9%
Femoral neck	1.033	4.3%	0.875	3.1%
Trochanter	0.884	2.2%	0.798	3.2%
Ward's triangle	0.852	7.3%	0.709	2.9%

Table IV. Effect of varying the location of the femoral neck box on femoral neck BMD in two normal volunteers (BMD values are mean results derived by averaging scans from 13 QDR-1000 systems)

Location of femoral neck box	Volunteer 1 Mean BMD (g/cm^2)	Volunteer 2 Mean BMD (g/cm^2)
Middle of femoral neck (normal placement by hip analysis software)	1.072	0.901
Adjacent to greater trochanter	0.986	0.861
Percentage change	8.0%	4.4%

3.5 Analysis by site radiographers

Results of independent analysis of the scans of the two volunteers by site radiographers were received for nine out of 13 QDR-1000 systems studied. The mean BMDs and their CVs are listed in Table III. The mean CV was 2.2% for the spine, 3.7% for the femoral neck, 2.7% for the trochanter and 5.1% for Ward's triangle. The most significant difference in analysis technique to emerge from this study was a variation in positioning of the femoral neck box. Some operators chose to leave this box in the location in the middle of the femoral neck selected by the hip analysis software, while others preferred to move the box until its lower lateral edge touched the upper medial border of the greater trochanter. Because of a relatively steep BMD gradient along the femoral neck, this difference in location can lead to significant differences in results. We therefore reanalysed all hip scans again ourselves, positioning the femoral neck box in each location. The resulting mean BMDs in the two positions for the two volunteers are compared in Table IV.

Table II. Mean BMDs and coefficients of variation (CV) for the spine and hip scans of two normal volunteers analysed using the Hologic scan comparison software

	Volunteer 1		Volunteer 2	
	Mean BMD (g/cm^2)	CV	Mean BMD (g/cm^2)	CV
Spine (L1–L4)	1.148	1.2%	1.171	1.6%
Femoral neck	1.072	1.9%	0.861	2.3%
Trochanter	0.881	1.6%	0.803	2.0%
Ward's triangle	0.842	2.7%	0.729	3.6%

4. Discussion

The most significant finding in this study was the close agreement between QDR-1000s when these were used to scan either the same phantom or the same human subjects. When sets of 10 sequential scans of a single Hologic spine phantom were acquired on different systems, the variations in mean BMD, BMC and Area were generally well within 1% (Fig. 1). Scans of two volunteers on different QDR-1000s gave CVs that averaged 1.4% for the lumbar spine and 2.1% for the femoral neck (Table II), figures only slightly larger than those expected for repeated scanning of an individual on a single system. These human data confirmed the findings of the phantom scans that any differences in calibration between sites must be less than or comparable with 1%.

During quantitative analysis of a scan the QDR-1000 system performs two functions: (i) the measurement of the projected area of bone within the analysis field; (ii) by comparison with the reference wheel, the mapping of BMD within that area. The third quantity calculated, BMC, is secondary, being obtained from the product of Area and mean BMD. There was a consistent trend during our study for Area measurements to show variations that were either minimal or below the detection threshold of our protocol, while BMD measurements showed larger variations significantly greater than our measurement threshold. The evidence for this consisted of the following findings.

(1) The CV between systems for the BMD measurement of a single spine phantom (0.58%) was significantly larger than that for Area (0.35%, $F = 2.7$, $p < 0.05$) (Fig. 1).

(2) The CV for the Area measurements performed on a single system (0.09%) was consistent with the measurement precision (0.12%). In contrast, the CV for BMD data from a single system (0.23%) was significantly larger than the precision (0.11%). As shown in Fig. 1(a), the larger than expected CV for BMD was due to a small change in calibration of around 0.4% towards the end of the study.

(3) When the results of our scans of site phantoms were compared with each site database, the root mean square deviation for the Area measurement (0.16%) was consistent with the precision (0.12%), while that for BMD (0.32%) was significantly larger than the figure expected (0.11%) (Table I).

(4) Further evidence for significant changes in system calibration came from a comparison of our BMC results for site phantoms with the Hologic nominal BMCs measured at factory calibration. As described in Section 2.1, this will reveal any changes in calibration since manufacture. The root mean square deviation found (0.32 g or 0.55%) was significantly larger than the study precision (0.08 g or 0.14%).

The advantage of repeated scanning of a Hologic spine phantom to characterize differences in calibration between different QDR-1000 systems was the high precision of the measurements (Table I). In contrast, the expected CV of around 1% for a lumbar spine measurement meant that our protocol of scanning only two volunteers was too insensitive to confirm in a statistically significant manner the differences in BMD calibration found from the phantom studies. Hence the human data confirmed that variations in BMD calibration are not greater than around 1%, but could not independently confirm the considerably smaller differences measured from the phantom data.

Our study allowed two further points of comparison between QDR-1000 systems: (i) an independent check of BMC differences between site phantoms; (ii) a comparison of site phantom database results. Our measurements of phantom BMCs gave differences from Hologic values of up to 0.5 g (0.9%), with a standard deviation of 0.29 g (0.5%). The CVs for the BMD results at site phantom databases ranged from 0.33% to 0.62%, a variation which is clearly statistically significant (Fig. 2). This result suggests that real differences exist in the stability of different systems.

Although this study has shown that differences in calibration between different QDR-1000 systems are less than 1%, it has also demonstrated that significantly larger variations can arise from differences in operator technique during scan analysis (Table III). While these should not affect the results of longitudinal studies conducted using the scan comparison software, they may be relevant when normal range data are being used. Our study has drawn attention to one particularly significant effect, the placement of the femoral neck box, which can cause differences of up to 8% (Table IV). Other common variations in technique which may significantly affect clinical results are the offset of the lateral edge of the hip analysis box from the greater trochanter, the width of the spinal analysis box and the treatment of transverse processes. While the finer details of technique are to a certain degree arbitrary, it is clearly important that a greater consensus is reached over analytical methods and that those who publish normal ranges should accurately describe the technique used.

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Patient dose and associated risk due to radiological investigation of the internal auditory meatus

By *J. J. Tweed, BSc, MSc, MIPSM, †M. L. Davies, BSc, MPhil, MIPSM, ‡K. Faulkner, BSc, PhD, ARCS, ‡D. J. Rawlings, BSc, MIPSM and ‡E. Forster, DCR, DHSA, BA

Regional Medical Physics Department, *North Riding Infirmary, Middlesbrough TS1 5JE, †South Cleveland Hospital, Middlesbrough TS4 3BW and ‡Newcastle General Hospital, Newcastle-upon-Tyne NE4 6BE, UK

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Abstract. The radiation doses and associated somatic risks due to four radiological examinations for acoustic neuromata (AN) have been investigated. These examinations were (1) plain film radiography of the internal auditory meatus (IAM), (2) computed tomography (CT) of the IAM, (3) CT of the posterior fossa and (4) CT of the IAM with air contrast. Organ dose measurements were performed using lithium fluoride thermoluminescent dosemeters loaded in a patient equivalent phantom. Dose equivalents to various organs are presented, together with the effective dose equivalent and collective effective dose equivalent for each examination. Hypothetical fatal somatic risks for each examination studied here have been estimated from the effective dose equivalents. The estimated number of hypothetical fatal cancers induced by radiological examinations for AN is between approximately 110 and 820 times lower than the number of detected AN, depending on the method of assessing the radiation dose to the remainder organs. It is concluded that in this particular study the radiological examinations are of net benefit to this group of patients.

Radiology of the internal auditory meatus (IAM) may occur several times in the diagnosis of acoustic neuromata (AN). Initially, three plain views are used to investigate erosion of the IAM, *i.e.* two oblique views, one of each petrous ridge (Stenver's projection) and one anteroposterior view showing both IAMs simultaneously viewed through the orbits of the eye. This may be supplemented by conventional tomography of the petrous bone or, more commonly, by computed tomography (CT). In CT of the IAM a contrast medium is used to demonstrate the presence of a space-occupying lesion in the cerobello-pontine angle. In the South Tees Health District, CT of the posterior fossa is routinely carried out in addition to CT of the petrous ridge (IAM) at the same test session. Final confirmation of the size and location of the neuroma is achieved by CT with air meatography.

In the 2-year period 1986–1987, 1094 patients were investigated for AN using plain radiographs. Of these, 164 patients had CT of the IAM and brain and 13 went on to have air meatography. All patients having air meatography were positively identified as having AN at surgery. Thus the number of patients who are found to have acoustic neuroma is small compared with those having initial plain view radiographic investigations. The radiological detection of AN using plain radiographs at this centre is approximately 40% (Flood et al, in press) which is similar to the detection rates at another centre (Singh et al, 1978). The detection rate for AN greater than 1.5 cm in diameter using CT at this centre is almost 90% (Flood et al, in press) and is comparable with experience elsewhere (Mikhael et al, 1987).

A number of workers have studied the radiation dose to the lens of the eye in radiological examination of the IAM (Montanara et al, 1986; English, 1988). Comprehensive data on radiation dose to other organs arising from these procedures are not readily available. The principal objective of this study was to determine the organ doses and associated hypothetical radiation risk arising from radiological examination of the IAM. This information is important in the objective assessment of the role of radiology in the investigation of the IAM.

Materials and methods

It was decided to perform a series of phantom measurements because normalized organ dose data for some of the IAM radiological examinations are not available. Absorbed dose measurements were made using the head of a Rando phantom (Alderson Research Laboratories Inc., Stamford, CT, USA) for the following radiological examination protocols: (1) a set of plain views, (2) CT of the IAM, (3) CT of the posterior fossa and (4) air meatogram CT. Technique factors for the exposures associated with these radiological examinations are summarized in Tables I and II. Radiographs were taken using Agfa Curix Ortho film with Ortho medium screen in conjunction with a focused grid with a grid ratio of 10:1 and strip density

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Address correspondence to Mr M. L. Davies, Regional Medical Physics Department, South Cleveland Hospital, Middlesbrough TS4 3BW, UK

*Present address: Audiology Department, Aberdeen Royal Infirmary, Woolman Hill, Aberdeen AB9 1GS, UK.

Table I. Technique factors for plain field radiographs on Philips Maximus C850

	Anteroposterior view	Oblique views
Field of view (mm)	130 × 65	60 × 75
Potential (kV)	82	80
Waveform	12 pulse	12 pulse
Focus to film (mm)	900	1050
Magnification	No	Yes
Grid	Yes	No
Auto density control	Yes	Yes
Milliamp second product	207	55
Entrance dose (mGy)	6.8	2.2

of 44 cm^{-1}. Values of elapsed mAs for corresponding radiographic examinations on several patients were noted using the post-exposure mAs meter and were found to be comparable with those noted for the Rando phantom. The Rando phantom was originally designed for use in radiotherapy and loses its tissue equivalence at low energies (Shrimpton et al, 1981). However, at the relatively high tube potentials used in the examinations studied here, it is considered that the Rando phantom will be approximately tissue equivalent. The CT scanner used in this study was a Technicare 2020 fourth generation machine using stationary detectors at half degree intervals. A shaped filter was used for IAM and posterior fossa scans; a flat filter was used for air meatography.

Lithium fluoride (LiF) thermoluminescent (TL) chips were placed at positions corresponding to the various organs and tissues of the head as shown in Table III. The positions of these organs within the Rando phantom were deduced from *Grant's Anatomy* (Basmajian, 1971) and the advice of a radiologist (Ruddle, 1986, Personal communication). These positions were the same as those used in an earlier study into the effective dose equivalent (EDE) received by staff in diagnostic radiology (Faulkner & Harrison, 1988). In addition, five strips of powdered LiF were positioned on the surface of the head parallel with the axis of the body so that they straddled the area of highest exposure. In all cases the radiographic examination protocols were repeated several times to increase the dose recorded and thereby reduce the effect on the results of uncertainty due to background readings.

The absorbed dose varies greatly through the phantom. In the case of plain field radiography it will be highest in the direct beam at the entrance surface and extremely low at remote points only reached by scattered radiation. In the CT examinations some or all of the following irradiations may take place: (1) a positioning or Delta view about 23 cm long, (2) a single scan for centralization purposes and (3) the series of scans from which the diagnosis will be made. Thus a complex dose distribution will exist from the high dose at the position of the centralization scan to the very low dose at points reached only by scattered radiation. Consequently, it was necessary to monitor organ doses using a number of TL devices as shown in Table III.

Organ and tissue doses

For the organs shown in Table III the dose was measured by distributing TL chips throughout the appropriate region in the Rando phantom. All doses are expressed as dose in tissue. For the sinuses and oesophagus, the TL chips were placed in contact with the surface of the respective organs. The arithmetic mean was used to specify organ doses. More chips were used for larger organs such as the brain than for smaller organs such as the pituitary, as shown in Table III. Doses to the lungs, breast and gonads arise solely from scattered radiation. The radiation dose levels to these organs from radiological examinations of the IAM were not measured because it was deduced from tables of normalized organ dose data that they were negligible (Drexler et al, 1985).

The red bone marrow (RBM) and bone surfaces are widely distributed throughout the body. Since only the head and neck are irradiated directly there is considerable variation of dose throughout the above organs or tissues. The doses to the RBM and bone surfaces were estimated using data collected by Huda and Sandison (1984) for the distribution of these organs throughout the Rando phantom. To calculate the dose to any of these organs or tissues, the average surface dose A_n, in

Table II. Technique factors for CT on Technicare 2020

	Delta view	IAM	Posterior fossa	Air meatography
Delta view used		Yes	No	Yes
Centralization scan		Yes	No	No
Number of diagnostic scans		14	10	13
Slice width (mm)	2	2	10	2
Table increment (mm)		2	10	2
Scan diameter (mm)	500	250	250	125
Potential (kV)	120	120	120	120
Tube current (mA)	30	75	50	75
Filter	Flat	Shaped	Shaped	Flat
Time per scan (s)	10	8	8	8

Table III. Regions of the Rando phantom monitored by TL dosemeter chips

Region	Number of TL dosemeters
Brain	14
Eyes	2
Sinuses	5
Parotid	6
Pharynx	1
Larynx	2
Oesophagus	9
Thyroid	2
Pituitary	1

Rando slice R_n, is multiplied by Huda and Sandison's F number F_n for that slice. F_n represents the proportion of that organ or tissue under consideration which is within the slice.

The average dose throughout the RBM and bone surfaces was estimated by summing over the Rando slices, from 1 to N, which were directly irradiated during each separate radiological examination. This is referred to as the direct dose. The small dose due to scattered radiation in the remainder of the body was ignored

$$\text{direct dose (organ)} = \sum_{1}^{N} A_n F_n \text{(organ)} \qquad (1)$$

The F numbers for bone represent the mass proportion of the bone whereas the quantity of importance is the top 10 μm layer of the bone surface (Wall et al, 1988). In this work it is assumed that the radiation doses to the bone mass and the bone surface are approximately the same. This was considered to be an acceptable approximation since the contribution of bone dose to the EDE is generally not more than a few per cent.

The EDE was calculated for each investigation using organ weighting factors (ICRP, 1977), using:

$$H_E = \sum_{T} W_T D_T Q N \qquad (2)$$

where H_E is the EDE, W_T is a weighting factor for that organ or tissue, D_T is the mean dose in organ or tissue T, Q is the quality factor and N is the product of all other modifying factors. For diagnostic radiology, Q and N are both unity.

In calculating the EDE, the contribution of the remainder organs was assessed using two different methods. Firstly, the method suggested by the ICRP (1977) was used, in which the dose equivalent to the next five organs with the highest dose was multiplied by 0.06 for each organ. Secondly, the method of Huda and Sandison (1984) was used, in which the average dose to all remainder organs is multiplied by 0.3. In this later method, the average dose to a slice in the Rando phantom is multiplied by Huda and Sandison's F number for the remainder organs in that slice. This value is summed over all slices and then multiplied by 0.3.

The EDE is a quantity where both the somatic and genetic effects are considered. In order to estimate the hypothetical fatal somatic risk from the EDE, the contribution of the gonads should be removed since the gonad dose only contributes to genetic effects. It is necessary to renormalize the EDE, by multiplying by 1/0.75, since the sum of the weighting factors for somatic effects only amounts to 0.75. This is because the weighting factor for genetic effects arising from the gonad dose is 0.25. However, for all the radiological examinations studied here, the weighted contribution of the gonad dose to the EDE was negligible. It was therefore possible to multiply directly the normalized EDE by the risk factor for fatal cancer induction. A value for this factor of 4.5×10^{-2} Sv^{-1} for the lifetime risk of fatal somatic effects averaged over the UK population of all ages and sex, was used as suggested by Stather et al (1988). This was drawn from a recent UNSCEAR report (1988) and takes into account changes in the projection models used to assess lifetime risk. As the radiation dose to the gonads for these investigations was negligible, so are the genetic effects. It has been suggested (Stather et al, 1988) that the risk of a radiation-induced non-fatal cancer is approximately half the risk of fatal cancers. It should be noted that the patients having radiological examinations for AN are relatively old when compared with the general UK population. Consequently, it is anticipated that the hypothetical risks quoted here will be overestimated.

Results and discussion

The results of the dose measurements and calculations together with weighting factors are shown in Table IV. It can be seen from Table IV that the highest doses occur in CT of the posterior fossa. It is anticipated that there will be some variation in radiation dose between patients; however, the main contribution arises from CT scanning in which the scan protocols used on different patients tend to be similar.

There has been some discussion in the scientific literature about the treatment of the remainder organs in the calculation of EDE (Huda & Sandison, 1988; Gibbs, 1989). It is because of the differing opinions that the EDE was calculated using the two methods. It is expected, for these particular examinations in which the head is irradiated, that the use of the ICRP method (1977) may lead to an overestimate in the assessment of the contribution of the remainder organs to the EDE, whereas using the method of Huda and Sandison (1984) may result in an underestimate of the EDE, as some organs in the head may be radiosensitive (Wall & Kendall, 1983).

The hypothetical risk of inducing a fatal cancer has been estimated from the EDE calculated using the two methods of treating the remainder. As there is some uncertainty in the value of EDE and risk factors for fatal somatic effects, there will also be uncertainty in the estimated hypothetical fatal somatic risks given in Table V. The hypothetical fatal somatic risks have, nevertheless, been estimated, as it is considered that

Table IV. Summary of mean organ doses (mGy)

Tissue	W_T	Plain radiography	CT IAM	CT posterior fossa	CT air meatogram
Thyroid	0.03	0.1	2.2	0.8	1.5
Brain	0.06	0.9	7.2	38.0	6.0
Pituitary	0.06	1.2	12.5	34.0	11.9
Sinuses	0.06	2.6	24.8	18.5	24.0
Parotid	0.06	0.3	7.6	2.0	8.0
Pharynx	0.06	0.1	2.9	0.9	1.5
RBM	0.12	0.1	1.7	3.5	2.1
Bone	0.03	0.1	1.7	3.5	2.1
Remainder[a]	0.30	0.04	0.5	1.0	0.7
Eyes	—	4.8	12.2	37.3	23.8

[a] Calculated using the method of Huda and Sandison (1984).

Table V. Summary of EDE and hypothetical fatal somatic risk

Examination	EDE (mSv)		Hypothetical fatal risk ($\times 10^{-6}$)	
	ICRP	Huda and Sandison	ICRP	Huda and Sandison
Plain radiography	0.32	0.03	19	2
CT IAM	3.6	0.48	220	28
CT posterior fossa	6.2	0.85	370	51
CT air meatogram	3.4	0.58	210	35

these data will be of assistance in the objective assessment of the role of radiology in the diagnostic of AN.

For a complete IAM investigation the total dose to the lens of the eye is 78.1 mGy. The dose to the eye from plain film radiography is 4.8 mGy which is higher than the value quoted by Montanara et al (1986). The dose to the eye due to CT of the posterior fossa is 37.3 mGy which agrees with the measurements of English (1988).

English points out that this dose can be reduced by a factor of 20 by angling the gantry to avoid direct irradiation of the eyes. However, the largest proportion of the total dose to the eyes is due to the posterior fossa scans which cannot be reduced by angling the beam. For all investigations the eye lens dose is low compared with the estimated threshold for lens opacification over a lifetime (ICRP, 1978).

Conclusion

It is worth noting that the most common radiological examination in the examination of AN (see Table VI) has the lowest dose. The collective effective dose equivalent (CEDE) has been determined by multiplying the number of patients for a given examination by the EDE. As may be deduced from Table VI, the contribution of plain radiography to the total CEDE for this group of patients is between 18% and 13%, depending on how the remainder dose is estimated.

Table VI. Summary of patient examinations and CEDE

Number of patients 1986–1987	CEDE (mSv person)	
	ICRP	Huda and Sandison
Plain radiography, 1094	350	33
CT IAM, 164	590	79
CT posterior fossa, 164	1010	140
CT air meatogram, 13	45	8

The data presented in Table V may be used to estimate the total number of hypothetical fatal cancers induced by radiological investigations of AN in the 2 year period 1986–1987. The number of induced hypothetical fatal cancers may be deduced by multiplying the total number of patients having a particular examination by the risk of a fatal somatic effect and then summing over all examinations. The estimated total number of hypothetical fatal cancers induced by radiological examination of AN is 0.12 using the ICRP method (1977) of treating the remainder organs and 0.016 using Huda and Sandison's method (1984). These are approximately 110 and 820 times lower than the number of AN detected (*i.e.* 13). Irrespective of how the dose to the remainder organs is treated, it may be concluded that these radiological investigations are of net benefit to this group of patients and are well justified.

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Monoenergetic approximation of a polyenergetic beam: a theoretical approach

By Donald M. Robinson, PhD and John W. Scrimger, PhD

Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta T6G 1Z2, Canada

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Abstract. There exist numerous occasions in which it is desirable to approximate the polyenergetic beams employed in radiation therapy by a beam of photons of a single energy. In some instances, commonly used rules of thumb for the selection of an appropriate energy may be valid. A more accurate approximate energy, however, may be determined by an analysis which takes into account both the spectral qualities of the beam and the material through which it passes. The theoretical basis of this method of analysis is presented in this paper. Experimental agreement with theory for a range of materials and beam qualities is also presented and demonstrates the validity of the theoretical approach taken.

A variety of materials have been used to construct beam modifying devices for use in radiation therapy. These range from low Z (atomic number) materials, such as wax, to high Z materials, such as lead. The use of these materials often requires the measurement of numerous broad beam attenuation coefficients sufficient to encompass the range of physical situations encountered (van Dyk, 1986). In a recent paper (Robinson & Scrimger, 1990) we presented an analytic technique for the design and fabrication of retracted missing tissue compensators based on primary and first-order scatter in which narrow beam attenuation coefficients are employed. Implicit to this approach is the assumption of a monoenergetic primary photon beam. The polyenergetic beams produced by linacs are often approximated by monoenergetic photons of energy equal to one third of the maximum spectral energy, according to a commonly invoked rule of thumb. This approach has proved successful for use with materials of low Z (wax, polystyrene and water) and intermediate Z (aluminium), but has yielded disappointing results with materials of high Z values such as lead. In this paper we present an analytical method for the determination of an appropriate effective energy for the monoenergetic representation of a polyenergetic beam in various materials based upon the spectral composition of that beam.

Theory

Let the continuous photon spectrum Φ_0 (photons per unit area)

$$\Phi_0 = \int_0^{E_{\max}} \phi(E)\,\mathrm{d}E \tag{1}$$

be approximated by a finite number N of spectral lines ϕ_i (photons per unit area) of energy E_i (MeV) such that

$$\Phi_0 = \sum_{i=1}^{N} \phi_i(E_i) \tag{2}$$

After passing through a thickness t of matter the above beam will be attenuated according to

$$\Phi = \Phi_0 \exp(-\mu_{\text{eff}}t) = \sum_{i=1}^{N} \phi_i(E_i)\exp(-\mu_i t) \tag{3}$$

where μ_{eff} is the effective attenuation coefficient for the polyenergetic beam and μ_i is the attenuation coefficient for photons of the ith spectral line energy. Dividing through by Φ_0 one obtains

$$\begin{aligned}\exp(-\mu_{\text{eff}}t) &= \sum_{i=1}^{N} \frac{\phi_i(E_i)}{\Phi_0}\exp(-\mu_i t)\\ &= \sum_{i=1}^{N} a_i \exp(-\mu_i t)\end{aligned} \tag{4}$$

where

$$a_i = \frac{\phi_i(\mathrm{E}_i)}{\Phi_0} \tag{5}$$

are the relative weights of the individual spectral components. Thus one has

$$\exp(-\mu_{\text{eff}}t) = \sum_{i=1}^{N} a_i \exp(-\mu_i t)$$

or

$$-\mu_{\text{eff}}t = \ln\left[\sum_{i=1}^{N} a_i \exp(-\mu_i t)\right] \tag{6}$$

and hence the effective attenuation coefficient for the beam becomes

$$\mu_{\text{eff}} = \frac{-1}{t}\ln\left[\sum_{i=1}^{N} a_i \exp(-\mu_i t)\right] \tag{7}$$

The effective attenuation coefficient defined by eqn (7) may be used to determine an effective single energy E_{eff} from tables of narrow beam attenuation coefficients, such as that produced by Hubble (1969) to characterize the beam.

Table I. Theoretical and experimental mass attenuation coefficients and effective monoenergetic energies

Material	Parameter	Beam energy					
		Cobalt 60		6 MV		15 MV	
		Theory	Experiment	Theory	Experiment	Theory	Experiment
Polystyrene, $\bar{Z} = 5.74$	μ/ρ (cm^2/g)	0.0639	0.064 ± 0.002	0.0494	0.049 ± 0.002	0.0348	0.035 ± 0.002
	E_{eff} (MeV)	1.16	1.14 ± 0.07	1.90	1.92 ± 0.12	3.60	3.54 ± 0.35
H_2O, $\bar{Z} = 7.51$	μ/ρ (cm^2/g)	0.0661	0.067 ± 0.002	0.0512	0.051 ± 0.002	0.0365	0.037 ± 0.002
	E_{eff} (MeV)	1.15	1.13 ± 0.07	1.89	1.91 ± 0.13	3.57	3.55 ± 0.36
Aluminium, $Z = 13$	μ/ρ (cm^2/g)	0.0574	0.056 ± 0.002	0.0456	0.046 ± 0.002	0.0338	0.034 ± 0.002
	E_{eff} (MeV)	1.15	1.22 ± 0.08	1.83	1.82 ± 0.15	3.37	3.30 ± 0.030
Lead, $Z = 82$	μ/ρ (cm^2/g)	0.0615	0.060 ± 0.002	0.0520	0.052 ± 0.002	0.0480	0.049 ± 0.002
	E_{eff} (MeV)	1.18	1.20 ± 0.04	1.61	1.60 ± 0.04	1.84	1.81 ± 0.04

The decay of cobalt 60 produces two energies of photons (1.17 and 1.33 MeV) which are often regarded as monoenergetic with an energy of 1.25 MeV. It is well known, however, that the output from a cobalt 60 treatment unit includes a low energy contamination component arising from scatter both from within the source itself and from the collimation system, and thus the output of a cobalt 60 unit is polyenergetic and amenable to an analysis of this type. This scatter component has been measured (Scrimger & Cormack, 1963) and may be characterized by 250 keV photons which contribute approximately 5% of the primary output of such a unit.

The spectral distribution of the 6 MV photon beam produced at this institute may be represented by the five spectral energies 1, 2, 3, 4 and 5 MeV with relative weights of 0.3730, 0.2516, 0.1842, 0.1261 and 0.0651, respectively. The 15 MV beam may be approximated by the seven spectral energies 1, 3, 5, 7, 9, 11 and 13 MeV with relative weights of 0.241, 0.188, 0.1566, 0.1325, 0.1181, 0.0988 and 0.065, respectively. The characterization of these beams is based upon the work of Sandifer and Taherzadeh (1968) and Mackie (1984). Resolution of the beams to a degree greater than presented above was not seen to yield appreciably improved results, while lower resolutions served to obscure pertinent beam detail, yielding poorer results.

Application of eqn (7) to the materials water, polystyrene, aluminium and lead using the above spectral distributions yields the theoretical effective narrow beam mass attenuation coefficients listed in Table I. The monoenergetic photon energies corresponding to these attenuation coefficients, as determined from Hubble (1969), are also listed in Table I. Experimental values of t in eqn (7) for water, polystyrene, aluminium and lead are 4.0, 4.4, 1.98 and 1.28 cm, respectively, the last three values being dictated by laboratory availability.

Experimental analysis

In order to verify the theoretical predictions presented above, the narrow beam attenuation coefficients for the materials of Table I were measured experimentally with cobalt 60, 6 MV and 15 MV photons. Measurements were taken at various field sizes and a representative plot is shown in Fig. 1 for polystyrene. Narrow beam linear attenuation coefficients were then determined by graphical extrapolation to zero field size using a third-order polynomial best fit as shown. The experimental values obtained in this manner are listed in Table I. In all cases theoretical and experimental attenuation coefficients are seen to agree within experimental error, as do their corresponding effective monoenergetic energies.

At each incident beam energy the effective monoenergetic energies for polystyrene, water, and aluminium are equal within the limits set by experimental error. This agreement extends to lead, however, only with cobalt 60. At 6 MV and 15 MV the effective energy for lead is less than that for the other three materials. This difference is most significant at 15 MV where the effective energy ranges from 3.55 to 1.81 MeV.

Although copper and tin were not available for

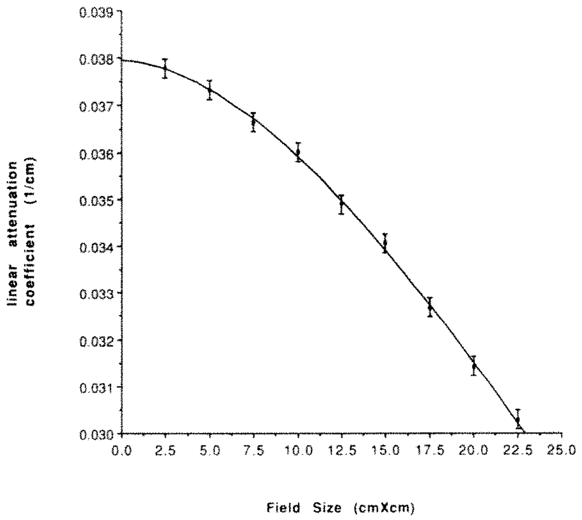

Figure 1. A plot of linear attenuation coefficient as a function of field size for polystyrene at 15 MV.

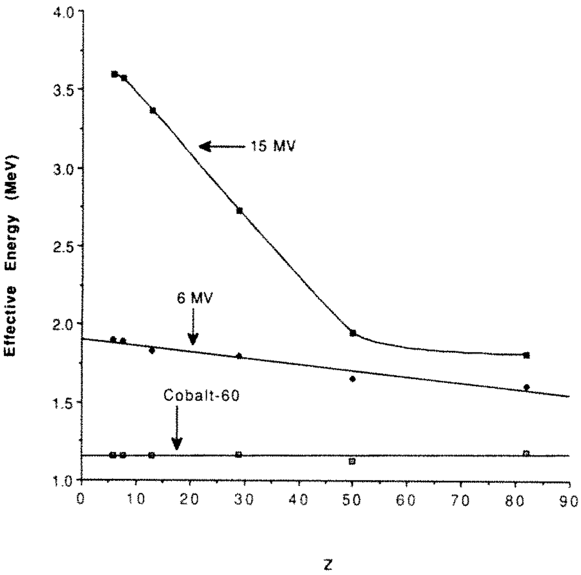

Figure 2. Theoretical effective energy (MeV) as a function of atomic number Z for cobalt 60, 6 MV and 15 MV photon beams.

experimental verification, the effective energies for 2 cm of both these materials were calculated and appear in Fig. 2. Here, theoretical effective energy is plotted as a function of atomic number Z for polystyrene ($\bar{Z} = 5.74$), water ($\bar{Z} = 7.51$), aluminium ($Z = 13$), copper ($Z = 29$), tin ($Z = 50$) and lead ($Z = 82$). From this graph one can see that for cobalt 60 photons the effective energy is relatively independent of atomic number, while for energies of 6 MV and 15 MV the effective energy is a decreasing function of Z. This Z dependency is most pronounced for 15 MV photons.

Discussion

The interplay between the contributing interaction cross-sections causes the total attenuation coefficient of a material to decrease initially as the photon energy increases, pass through a minimum, and then increase as the photon energy is increased further. The energy of minimum attenuation decreases as the atomic number increases. The chief contributor to this energy shift is pair production. With low Z materials, such as H_2O, the compton interaction predominates over the range of energies investigated. For high Z materials, however, the contribution from pair production becomes significant in the case of 6 MV, and predominant in the case of 15 MV, for the higher energy spectral components of these beams. The contribution of these high energy spectral components serves to cause the effective mono-energetic energy of these beams to decrease as Z increases, as demonstrated in Fig. 2.

Thus, when approximating a polyenergetic photon beam with monoenergetic photons, care must be taken in the choice of photon energy used. Commonly used rules of thumb may be appropriate in some circumstances, but a more accurate analysis must take into account the spectral qualities of the beam and the material through which it passes. This is most important for high Z materials, which find common use in compensator construction in many centres, when used in high energy beams. A system involving different materials may require a different energy for each material encountered by the beam. The approach presented in this paper allows for the accurate prediction of an appropriate energy based upon such considerations. Agreement with experiment validates the theoretical approach taken for the range of materials investigated.

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Cancer risk among staff at two radiotherapy departments in Denmark

By *Michael Andersson, MD, †Gerda Engholm, §Klaus Ennow, MSc, ‡Karl A. Jessen, PhD and †Hans H. Storm, MD

Department of Oncology, Finsen Institute/Copenhagen University Hospital, Denmark, †Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Rosenvængets Hovedvej 35, Box 839, DK 2100 København Ø, Denmark, §National Institute of Radiation Hygiene, National Board of Health, Frederikssundsvej 378, DK 2700 Brønshøj, Denmark and ‡Department of Medical Physics, Aarhus Municipal Hospital, DK 6000 Århus, Denmark

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Abstract. In comparison with the general Danish population, the relative risk (RR) for cancer among staff members employed in two radiotherapy departments in Denmark during 1954–1982 and alive on 1 April 1968 was assessed by linkage to the Danish Cancer Registry. All staff had been monitored with film dosimeters for exposure to radiation. The study cohort consisted of 4151 persons, accruing 49553 person-years at risk. The collective radiation dose was 76.54 manSv and the mean dose 18.4 mSv. A total of 163 cancer cases were observed with 152.3 expected. The risks for cancers usually considered to be radiogenic were not elevated. A significant excess of prostatic cancer was observed (five cases, relative risk, 6.02; 95% confidence interval, 1.94–14.06); this is likely to be a chance finding. No relation was observed between radiation dose or years of exposure and cancer risk, but a weak non-significant increase in risk with time since first exposure was seen.

The carcinogenicity of ionizing radiation to humans is indisputable. Our understanding of human radiocarcinogenesis stems mainly from studies of populations exposed to relatively high doses of external radiation received at a high dose rate. Populations exposed in this way are the Japanese A-bomb survivors and patients who were given medical radiation for a variety of conditions in the past.

These populations have been followed extensively in order to increase our understanding of radiation carcinogenesis by studying dose-response, temporal and age relations and application of the findings to the lower dose range (UNSCEAR, 1988). Numerous epidemiological studies of nuclear workers have shown that there is no consistent excess risk for cancer in general or for cancers at specific sites (Gilbert & Marks, 1979; Rinsky et al, 1981; Beral et al, 1985; Checkoway et al, 1985; Smith & Douglas, 1986; Wilkinson et al, 1987; Beral et al, 1988). Findings from these studies are in agreement with the dose-response relationships commonly employed, when taking into account the relatively small doses and limited population sizes. The risk estimates were extrapolated from the high dose range to lower doses under the assumption of a linear or linear-quadratic relationship, with no threshold dose for carcinogenesis, applying both additive and multiplicative risk models (UNSCEAR, 1988).

Large populations in modern society are potentially exposed to very low dose radiation either in occupational settings, *e.g.* in the nuclear industry and in the medical practice, or domestically from radon; even larger populations may be exposed as a result of accidental emissions of nuclides from nuclear plants (Anspaugh et al, 1988). Few studies have been carried out to assess the cancer risk among potentially irradiated medical staff. In a number of investigations of UK and US radiologists, elevated risks for leukaemia and multiple myeloma were observed when they were compared with those of physicians in other specialities and of the general population (Ulrich, 1946; March, 1950; Court Brown & Doll, 1958; Lewis, 1963; Seltser & Sartwell, 1965, Warren & Lombard, 1966; Smith & Doll, 1981; Matanoski et al, 1984). However, in the past all radiologists were probably rather heavily irradiated. In a recent study 27011 diagnostic X-ray workers in China (physicians as well as technicians), some of whom were rather heavily irradiated, had elevated risks for leukaemia and cancers of the skin, breast and thyroid when compared with physicians who did not use X-rays in their work (Wang et al, 1988).

In Denmark, by far the largest group of persons in medical practice who are potentially irradiated actually work in diagnostic radiology. The highest collective and average radiation doses, however, are measured among staff at radiotherapy departments (National Institute of Radiation Hygiene, 1982). We therefore considered it of interest to study cancer risk in relation to measured radiation dose in a cohort of 4151 persons working in two radiotherapy departments from 1954 to 1982 and alive on 1 April 1968.

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*Author for correspondence. Present address: The Danish Cancer Registry.

Materials and methods

More than half the radiotherapy for cancer in Denmark during the period 1954–1982 was given in the departments of oncology at the Finsen Institute in Copenhagen or at Aarhus Municipal Hospital. Treatment modalities included high voltage external beam therapy with cobalt 60 or linear accelerators which were used for a variety of cancers, intracavitary therapy with sealed sources of radium 226, cobalt 60 or caesium 137 for gynaecological cancers, and internal iodine 131 therapy for thyroid cancer.

Since 1954, persons considered to be at risk of exposure to radiation have been monitored at both centres using personal film dosimeters. The dosimeters were calibrated to measure the skin dose at the position of the dosimeter, which should be on the front of the trunk. The measurements were converted to whole body dose equivalent by a single factor independent of the photon energy: 1 mGy equals 1 mSv. From the results of an intercomparison of dosimeter measurements in the Nordic countries this conversion will possibly overestimate the effective dose equivalent by up to 50% taking into consideration the actual radiation conditions (Ennow et al, 1985). During the period 1954–1975, radiation dose monitoring was performed within the two radiotherapy departments, and the results, in terms of measured annual radiation doses for each person, were kept on card files together with the name, date of birth and occupation. Since 1975, monitoring has been centralized at the National Institute of Radiation Hygiene and the results have been computerized. Information from the two sources was then linked on computer files. On the basis of name, date of birth and occupation, each individual was sought by linkage to the Central Population Registry, union rosters and salary rosters to obtain the unique personal identifying number given to all inhabitants of Denmark on 1 April 1968. Only persons who were fully identified by record linkage were included in the study, excluding all those not alive on 1 April 1968. Vital status on 31 December 1985 of persons in this cohort was obtained by record linkage with the Central Population Registry utilizing the identifying number.

Cancer cases diagnosed in the cohort between 1 April 1968 and 31 December 1985 were identified by record linkage to the Danish Cancer Registry. Since 1943, this registry has received reports on cancer cases from hospital departments, pathology departments and general practitioners on a national basis and combined the information with that from all death certificates issued in the country. The registry is considered to be extremely complete and accurate (Storm, 1988).

The expected numbers of cancers were calculated by applying the appropriate number of person-years at risk to cancer incidence rates from the Danish Cancer Registry specified for age (5-year intervals), sex, calendar period (5-year intervals) and cancer site (according to a modified version of the ICD-7) (Danish Cancer Registry, 1988). Each individual was considered to be at risk from 1 July of the year of first dose measurement (or 1 April 1968 if the first measurement was performed before this date) until death, emigration or 31 December 1985. The computations were performed by means of the PYRS programme (Coleman et al, 1986). Confidence intervals (CI) for the ratio between observed and expected numbers of cancer cases were calculated by treating the observed number of cases as a Poisson variable with a mean equal to the expected number times the excess cancer risk (Berry, 1983). Byars limits were used (Rothman & Boice, 1982).

Results

Altogether, 4151 persons (82% women and 18% men) accruing 49553 person years at risk were available for the study. The characteristics of the cohort are given in Table I. The smallest group, radium packers, was employed in loading the devices for intracavitary therapy with radium 226, cobalt 60 and caesium 137. They, together with nurses handling these devices, received the largest radiation doses. Most persons were in the age group 20–34 years when their first dose measurement was performed. The majority had had measurements for fewer than 3 years, and only 15% for more than 6 years.

The accumulated radiation doses were relatively low,

Table I. Characteristics of 4151 persons monitored for exposure to radiation

	Number of persons	Per cent
Profession		
Nurse	1735	42
Radium packer	106	3
Physician	700	17
Technician	227	5
Others[a]	1383	33
Age at first exposure (years)		
< 20	84	2
20–34	2938	71
35–49	869	21
⩾ 50	260	6
Length of exposure (years)		
< 3	2537	61
3–5	972	23
⩾ 6	642	15
Cumulative dose (mSv)		
None	723	17
0–5.00	1930	46
5.01–50.00	1144	28
⩾ 50.01	354	9

[a] Includes radiophysicists, radiographers, laboratory technicians, secretaries and some nurses not properly identified as such.

Table II. Observed numbers and relative risks for cancer in relation to measured cumulative radiation dose

Cancer site	Dose (mSv)										
	0 (5580)[a]		0.01–5.00 (21906)		5.01–50 (16395)		≥ 50.01 (5672)		Total (49553)		
	Observed numbers	Relative risk	Observed numbers	Relative risk	Observed numbers	Relative risk	Observed numbers	Relative risk	Observed numbers	Relative risk	95% CI
All malignancies	12	1.14	43	0.90	72	1.27	36	0.96	163	1.07	0.91–1.25
All sarcomas[b]	1	6.67	1	1.43	0	—	1	2.38	3	1.51	0.30–4.40
Digestive organs	1	0.74	6	0.89	10	1.07	4	0.50	21	0.82	0.51–1.26
Respiratory system	2	2.66	6	1.61	4	0.78	4	1.20	16	1.24	0.71–2.01
Breast	5	1.98	9	0.81	21	1.64	9	1.17	44	1.29	0.93–1.73
Cervix uteri	0	—	2	0.41	3	0.61	2	0.84	7	0.52	0.21–1.08
Corpus uteri	1	2.25	3	1.70	3	1.14	1	0.48	8	1.16	0.50–2.28
Ovary	1	1.90	2	0.88	3	1.04	2	1.00	8	1.04	0.45–2.05
Prostate	0	—	0	—	3	8.11	2	8.53	5	6.02	1.94–14.06
Kidney	0	—	0	—	3	2.36	0	—	3	0.90	0.18–2.63
Bladder	1	4.76	3	2.63	1	0.63	2	1.71	7	1.71	0.68–3.52
Skin	1	0.62	5	0.72	14	1.90	5	1.13	25	1.23	0.80–1.81
Thyroid	0	—	1	2.08	0	—	0	—	1	0.81	0.11–5.75
Brain, nervous system	0	—	2	1.09	4	2.23	1	1.08	7	1.40	0.56–2.89
Lymphoma	0	—	0	—	0	—	1	1.35	1	0.27	0.00–1.48
Multiple myeloma	0	—	1	4.00	1	2.63	1	2.94	3	2.99	0.60–3.77
Leukaemia	0	—	1	1.09	1	0.98	0	—	2	0.70	0.08–2.54
Other	0	—	2	0.64	1	0.28	2	0.85	5	0.54	0.22–1.30

CI, confidence interval.

[a] In parentheses, person-years at risk.

[b] Also included in site-specific categories below.

Table III. Observed numbers and relative risks for cancer in relation to number of years of radiation dose measurement

Cancer site	1–2 years (28779)[a]		3–5 years (11046)		≥ 6 years (9728)	
	Observed numbers	Relative risk	Observed numbers	Relative risk	Observed numbers	Relative risk
All malignancies	75	1.04	28	0.92	60	1.21
All sarcomas[b]	2	1.98	0	—	1	1.72
Digestive organs	11	0.98	2	0.44	8	0.82
Respiratory system	8	1.36	3	1.18	5	1.11
Breast	20	1.21	9	1.26	15	1.43
Cervix uteri	4	0.57	1	0.35	2	0.58
Corpus uteri	2	0.68	1	0.75	5	1.88
Ovary	4	1.13	0	—	4	1.53
Prostate	2	5.98	1	6.59	2	5.84
Kidney	2	1.34	1	1.61	0	—
Bladder	4	2.16	1	1.32	2	1.33
Skin	9	0.89	6	1.43	10	1.65
Thyroid	0	—	1	3.85	0	—
Brain, nervous system	3	1.17	1	0.95	3	2.21
Lymphoma	0	—	0	—	1	0.95
Multiple myeloma	1	2.33	0	—	2	4.88
Leukaemia	1	0.72	0	—	1	1.10
Other	4	0.77	1	0.56	0	—

[a] In parentheses, person-years at risk.
[b] Also included in site-specific categories below.

Table IV. Observed numbers and relative risks for cancer in relation to time from first radiation dose measurement

Cancer site	0–9 years (27089)[a]		10–19 years (16534)		≥ 20 years (5930)	
	Observed numbers	Relative risk	Observed numbers	Relative risk	Observed numbers	Relative risk
All malignancies	43	0.92	69	1.13	51	1.15
All sarcomas[b]	1	1.30	2	2.59	0	—
Digestive organs	2	0.32	8	0.77	11	1.24
Respiratory system	4	1.30	3	0.60	9	1.86
Breast	14	1.31	19	1.34	11	1.19
Cervix uteri	2	0.36	4	0.71	1	0.47
Corpus uteri	4	2.13	3	1.09	1	0.44
Ovary	3	1.23	2	0.64	3	1.42
Prostate	0	—	2	8.12	3	6.55
Kidney	1	1.16	2	1.48	0	—
Bladder	3	3.03	4	2.46	0	—
Skin	4	0.62	14	1.77	7	1.17
Thyroid	1	1.90	0	—	0	—
Brain, nervous system	2	1.03	4	2.05	1	0.90
Lymphoma	0	—	0	—	1	1.15
Multiple myeloma	0	—	2	4.90	1	2.78
Leukaemia	2	2.06	0	—	0	—
Other	1	0.32	2	0.51	2	0.71

[a] In parentheses, person-years at risk.
[b] Also included in site-specific categories below.

as 63% of persons received accumulated doses of less than 5 mSv and only 9% more than 50 mSv; 16 persons received more than 500 mSv, and three persons more than 1 Sv. The total collective radiation dose was 76.54 manSv, and the average cumulated radiation dose was 18.4 mSv.

A total of 163 cancer cases were observed and 152.3 expected, giving a relative risk (RR) of 1.07 (Table II). The RR for cancer differed significantly from unity for only one site, prostate with a RR of 6.02. The five cases of prostatic cancer all presented with or developed to metastatic disease, and all occurred among men who had had their first dose measurement during 1954–1963. Two were in men between the ages of 20 and 34 years at first exposure and three were between 35 and 49 years old. Four cases occurred among physicians and the other in a hospital porter. Only two cases of leukaemia were observed *versus* 2.8 expected. Thyroid and breast cancer did not occur in significant excess. No obvious dose-response relationship with measured accumulated radiation dose was seen for cancer in general (Table II).

In order to account for any inaccuracy in the film dosimeter measurements or compliance of staff with use of the film badges, cancer risk was also assessed in relation to number of years of dose measurement (Table III). Again, in general no relationship with cancer was observed.

Period at risk since first dose measurement is another surrogate measure of cumulative radiation dose. Most of the measurements were made recently so that the latency (time from first measurement to death, emigration or end of observation period) was often short, exceeding 10 years for only 45% and exceeding 20 years for only 12% of the group (Table IV). In the RR for cancer in general, a non-significant increasing trend with time since first exposure was observed, with relative risks of 0.92 (95% CI, 0.66–1.24), 1.13 (0.88–1.43) and 1.15 (0.85–1.51) for risk periods of 0–9 years, 10–19 years and 20 years or more, respectively. However, for specific cancer sites this non-significant trend was observed only for digestive organs.

Discussion

Recently, much public concern has been expressed over the potential hazards of occupational and accidental exposure to ionizing radiation, and current estimates of cancer risk have been debated and revised (UNSCEAR, 1988). The present study is the first to address this question in relation to staff at radiotherapy departments.

The measured cumulative doses in the study cohort are relatively low, with an average of 18.4 mSv, which is approximately half the radiation absorbed from natural sources during the observation period. However, the measured radiation is unevenly distributed, as 17% received no measurable radiation and 9% received more than 50 mSv. The highest doses were measured among staff handling the devices for intracavitary therapy with radium, cobalt and caesium, especially during the earliest part of the study period. Since then, improved radiation hygiene and the introduction of afterloading techniques has drastically reduced exposure to radiation.

Possible limitations of radiation monitoring must be taken into consideration. First, the persons first employed before 1954 probably received substantial radiation doses, especially those employed in intracavitary therapy, although the magnitude of this exposure cannot be evaluated with any degree of certainty. However, this is probably not of great importance as only 126 persons had their first dosimeter measurement in 1954, even though the mean cumulated dose for these persons in the years following is as high as 175 mSv. Second, the accuracy of film badge monitoring may be questioned, especially during the earliest years. Finally, the compliance of individual staff members for carrying the film badges in all work situations, when changing coats and operating gowns, and the use of lead aprons, cannot be ascertained.

The present study demonstrated that there was no excess risk for cancer, in accordance with the results of most studies of occupationally exposed cohorts, especially in the nuclear industry. If current estimates of cancer risks derived from the studies of Japanese A-bomb survivors of approximately 10 per 100 per Gy (UNSCEAR, 1988) are applied to the present study, an excess of eight cancers due to occupational exposure to radiation would have been anticipated. This estimate is debatable, however, for many reasons, including the uncertainties about radiation dose measurements, linear extrapolation from high dose radiation with high dose rate to low dose radiation with low dose rate, lack of consideration of age at exposure and time since exposure, lack of lifelong follow-up and the use of an additive instead of a multiplicative model for projecting the radiation risk. The statistical power of the study is limited, and only a 25% excess of cancer can be ruled out with reasonable certainty.

The only cancer site for which there was a significant deviation from the expected number was the prostate. This is most probably a chance finding. It is unlikely to be due to greater surveillance of the cohort compared with the general population as all five cases either initially presented with, or later developed, osseous dissemination and would thus have been diagnosed in any situation. One explanation for the increased risk could be that the general population is not the best comparison group, since prostatic cancer is observed in excess among men in higher social classes (Ross et al, 1979). We were unable to account for social class in our analysis; however, four of the five cases were found among physicians. Prostatic cancer is not usually considered to be a radiogenic cancer (Committee on the Biological Effects of Ionizing Radiation, 1980), and mortality from this cancer does not appear to be related to exposure to radiation in the large studies of survivors from the nuclear explosions in Japan. However, incidence data from the Nagasaki Tumour Registry (including both clinical and subclinical cases) point to radioinducibility, with an absolute risk of 2.1 cases per

10 000 per Gy (UNSCEAR, 1988). Interestingly, several studies of nuclear workers, especially those of workers from the UK, have demonstrated elevated risks of cancer of the prostate, sometimes associated with a positive dose-response relation (Beral et al, 1985; Checkoway et al, 1985; Smith & Douglas, 1986; Wilkinson et al, 1987; Beral et al, 1988).

In most studies of nuclear workers, a so-called "healthy worker effect" has been demonstrated, with lower RRs for both non-malignant deaths and, to a lesser extent, deaths due to malignant diseases. This effect has been attributed at least partially to a significant deficit of tobacco-related cancers among nuclear workers, who are subjected to repeated medical examinations and restrictions on smoking during working hours (Mole, 1987). In our study, no healthy worker effect was demonstrated (RR for cancer, 1.07). This may be due to the different smoking habits of medical staff compared with nuclear workers, as is indicated by the RR for respiratory cancer of 1.24 in our study in contrast to a significantly low risk in studies of nuclear workers.

The findings in our study should be interpreted with caution as the study is small, follow-up for many cohort members is limited and the measured doses are low. However, the absence of excess risks for accepted radiogenic cancers (leukaemia, breast, thyroid) supports the current risk estimates for radiation induced cancer, even though we cannot rule out an overall 25% excess and for some sites a more than twofold excess, or conversely a protective effect of work in these environments.

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Technical note

Fast personal computer based retrieval system for a high-volume database of a radiology information system

By *Reinhard Urhahn, PhD and Rolf W. Günther, MD

Department of Diagnostic Radiology, Technical University of Aachen, Pauwelsstrasse, W-5100 Aachen, FRG

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Keywords: Personal computer, Database retrieval, Radiology information system

Abstract. A personal computer system has been used to facilitate search and analysis of a radiology information system database (RADOS) for research purposes. The system enables flexible retrieval of examination data and radiographic findings with subsequent graphical manipulations. With modifications it could be implemented on other radiology information systems.

A growing number of radiology departments today use commercially available computerized radiology information systems (RIS) for departmental management. They are designed to manage such functions as patient registration, examination scheduling or diagnostic reporting. In addition, some systems support retrieval functions for research purposes. However, the retrieval software is often insufficiently adapted to the specific needs of the user. For example, graphical representation of retrieved data is not possible.

Because of increased demand for medical database retrieval we linked a personal computer (PC) to our department's RIS (RADOS) and developed appropriate software for the transfer and analysis of selected examination data. Our objective was to facilitate both database search and manipulation of retrieved information. The system design and performance are the subject of this article.

Methods

The RIS installed is an information system (RADOS, Philips) based on a MicroVAX II computer, used to manage about 130 000 examinations annually. The PC is a commercially available microcomputer system (Atari 1040STF) including a hard disk and a high-resolution graphic monitor. At present the PC is connected with the VAX via an RS232C interface with a maximum data transfer rate of 19200 Baud. A high-speed Ethernet network will be available for the PC in the near future. Data transfer is performed by PC resident I/O routines activating VAX resident standard functions of the RADOS archive menu to collect and transmit selected data.

The menu-driven PC software (compiled in BASIC) comprises the following procedures: (a) Transfer/sort, (b) pre-scan and (c) main-scan.

Transfer/sort

This procedure creates a stand-alone database on the PC. The following basic patient and examination data of the RIS database are used: examination type and identification number, age and sex of the patient, referring clinical department and report status. The basic data are usually transferred quarterly from the RIS to the PC. After subsequent sorting by examination type they are stored in a random access file on the hard disk. An additional index file enables fast data access.

Pre-scan

This performs a search of the PC database, starting up with the input of the parameters "examination year(s)" and "examination type or group". Search restrictions to age groups, patient sex or referring departments are possible. The procedure generates a sorted list of the specified examinations and corresponding basic data of the PC database with additional statistics and diagrams (*e.g.* age distributions). All results may be hardcopied or graphically represented on the screen. On request the selected examination identification numbers are stored for later retrieval of radiographic findings.

Main-scan

This procedure enables retrieval of radiographic findings. Having transferred the pre-selected identification numbers to the VAX, the procedure receives corresponding basic demographic patient data and the data records for the free report text, clinical details and numeric codes for radiographic findings similar to the ACR code (American College of Radiology, 1975). During the transmission the data records are simultaneously checked for selected keywords and code numbers. The matching records are printed out or stored on disk in a standardized format for further analysis and manipulations such as individual graphical representation and establishment of teaching-file databases.

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*Author for correspondence.

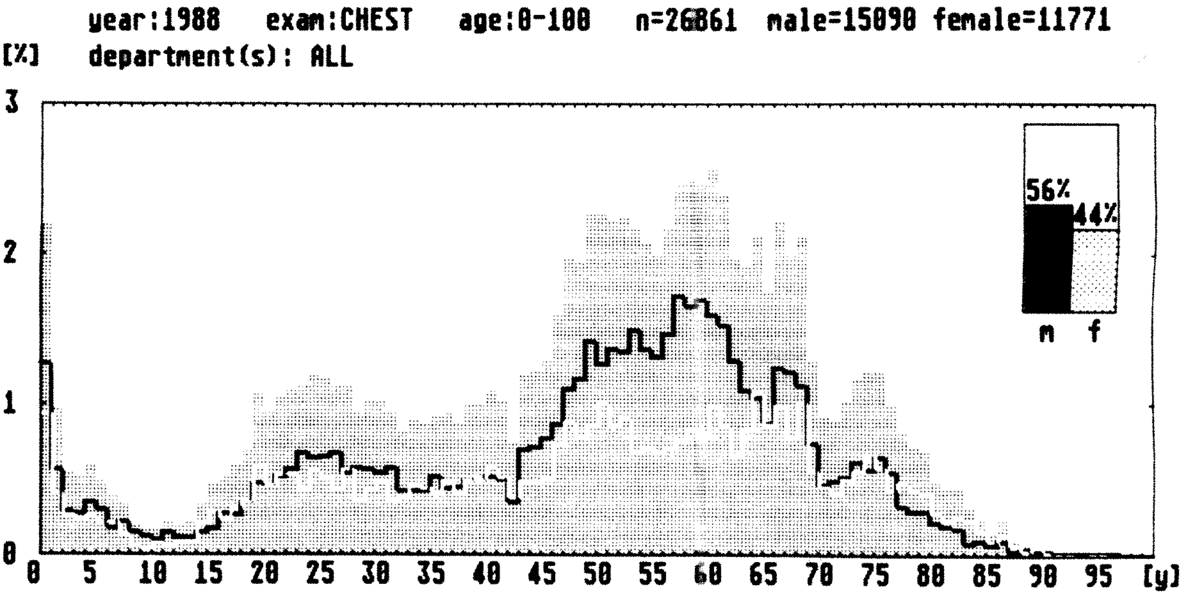

Figure 1. Graphical analysis of selected examination data: frequency of standard chest radiographs (%) versus patient age.

Results

The retrieval system has been in operation for 1 year. Typical execution times are transfer/sort 20 minutes (quarterly), pre-scan 5 seconds (search volume 1 year), main-scan 15 minutes (search volume 1 year).

Typical examples of application are shown in Fig. 1 and Table I. Figure 1 shows the frequency of chest radiographs versus patient age. In addition, the diagram shows the overall (inset) and age-dependent frequency for female (white lines) and male patients (black lines). The characteristics of the distribution depend on the morbidity and the demographic structure of the local population as well as on the clinical disciplines. The analysis of such distributions may be useful for the estimate of age-dependent radiation exposure.

The result of an analysis of radiographic findings is given in Table I. The free text of chest radiograph reports was searched for keywords such as "azygos lobe" or portions of the keyword with regard to typing errors. The overall incidence found for the azygos lobe agrees with the literature (Felson, 1973).

Discussion

Personal computers are useful for database management in an academic radiology environment (Kurtz et al, 1984; Sommer, 1986; Amis, 1987). The described PC-based retrieval system is a powerful low-cost supplement to a high-volume RIS, relieving the main computer of time-consuming search operations. The developed software allows fast transfer, analysis and graphical manipulation of examination data. Flexible retrieval of radiographic findings is performed by a code and keyword-based procedure including both search of free text and diagnosis code. The system could serve as a model for radiology departments equipped with information computers insufficiently provided with flexible retrieval software for research as well as clinical service. Unfortunately, most RIS systems use different standards for patient and examination data access and data format. Implementation of the system on a different RIS therefore requires some modifications of the data aquisition routines of the PC software. Technical details and programme source code are available from the authors on request.

Table I. Incidence of the accessory lobe of the azygos vein, keyword "azygos lobe" (1988–June 1989, standard chest examination)

	Female	Male	Total
Individuals	10087	11752	21839
Azygos lobe	40	67	107
Incidence (%)	0.40	0.57	0.49

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Case reports

Intraperitoneal pseudocyst formation as a complication of continuous ambulatory peritoneal dialysis

By J. Namasivayam, MRCP, FRCR

Department of Radiology, Western Infirmary, Glasgow G11 6NT, UK

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Keywords: Continuous ambulatory peritoneal dialysis, Sclerosing peritonitis

A patient with an intraperitoneal pseudocyst occurring as a complication of continuous ambulatory peritoneal dialysis (CAPD) for chronic renal failure is presented. The diagnosis was made pre-operatively by ultrasound. This has not been previously reported.

Case report

A 59-year-old man, with chronic renal failure maintained on CAPD for 1 year, presented with a painful tender mass in the left hypochondrium, which had increased rapidly in size over the previous 2 months. There was an associated history of weight loss, poor appetite and some impairment of ultrafiltration. At no stage did he complain of any bowel symptoms.

An ultrasound examination demonstrated a large unilocular encysted fluid collection, measuring 8 cm by 17 cm diameter (Fig. 1). The cyst was confined mainly to the left side of the abdomen and was anterior to the intra-abdominal organs. It had a uniform bright outline, indicating a pseudocapsule. The tip of the CAPD catheter was seen to lie within the collection (Fig. 2). Laparotomy confirmed the ultrasound findings and, in addition, there were changes suggestive of early sclerosing peritonitis (SP). The pancreas had a normal appearance at surgery. The cyst was drained and the fibrous capsule excised. The amylase content of the cystic fluid was normal. Ultrasound

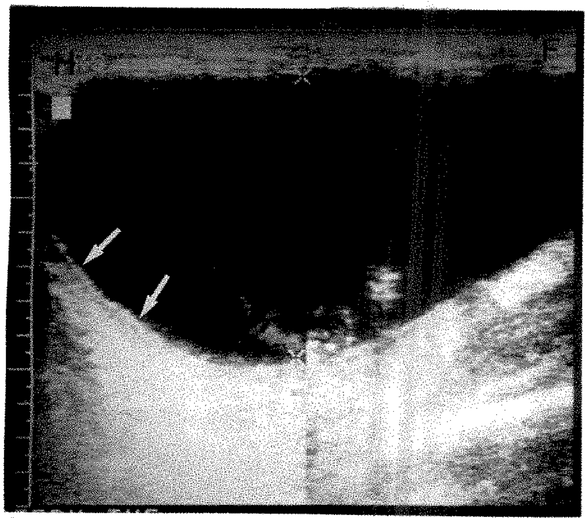

Figure 1. Sagittal section of the left upper quadrant of the abdomen, demonstrating a large unilocular cystic mass. The pseudocyst is outlined by a fibrous capsule (arrows).

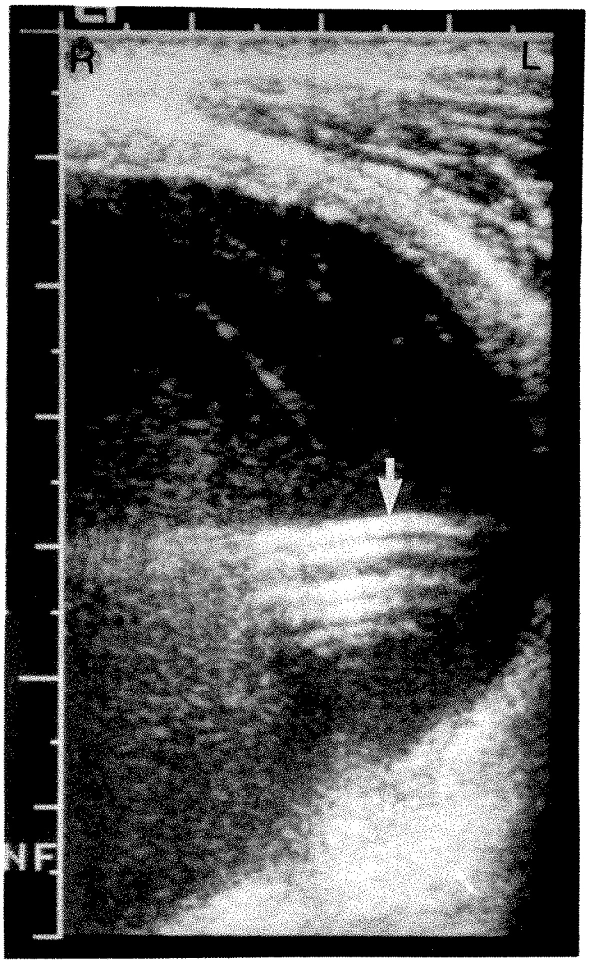

Figure 2. Transverse section of the left upper quadrant demonstrating the pseudocyst containing linear high amplitude double lumen representing CAPD catheter (arrow).

Address correspondence to: Dr J. Namasivayam, Department of Radiology, Royal Infirmary, Glasgow G4 0SF, UK.

examination following surgery disclosed no abnormality. The CAPD was discontinued and the patient received a successful renal transplant one week later. Following transplantation, his general condition improved dramatically.

Discussion

Continuous ambulatory peritoneal dialysis is an effective maintenance therapy for patients with endstage renal disease. However, it is not without risks and complications (Rottenbourg et al, 1983). In a patient on CAPD, the co-existence of pseudocyst formation and SP, as in this case, suggests a common underlying pathological process which is presumably governed by the same aetiological factors. Absence of bowel symptoms, lack of ultrasonographic changes of typical SP and dramatic clinical improvement following excision of the pseudocyst presumably indicate a mild form of SP which is localized. The association between pancreatitis and endstage renal failure and dialysis has been suggested (van Dyke et al, 1986), but in this case the pancreas was normal.

Sclerosing peritonitis is now a well recognized complication of CAPD. It is characterized by greatly thickened peritoneal membranes, which histologically have been transformed into dense layers of fibroconnective tissue infiltrated with mononuclear and polymorph cells (Gandhi et al, 1980). Sclerosing peritonitis tends to progress unrelentingly and is unaffected by cessation of CAPD therapy (Holland, 1990).

Intraperitoneal pseudocyst formation in association with ventriculoperitoneal shunt is a well recognized complication. The development of a fibrous capsule or cyst around the tip of the shunt is thought to result from a low grade infection and localized peritonitis (Fischer & Shillito, 1969). The cyst wall is composed of intestinal loops matted together by connective tissue (Nagakaki et al, 1979). It is presumed that a similar pathological process occurred in this case in association with CAPD. A localized fluid collection around the Tenckoff catheter is pathological and suggests localized peritonitis or a sterile inflammatory response to the catheter.

Recurrent peritonitis as a result of tunnel infection from a Tenckoff catheter has been reported (Joffe & Friedberf, 1985), and was thought to be related to abdominal pseudocyst formation around the subcutaneous peritoneal dialysis catheter, acting as a reservoir for bacteria. In this patient there was no tunnel infection at any stage, nor was there any clinical evidence of peritonitis. There was thus no need to change the catheter.

The cause of SP following CAPD is thought to be multifactorial. Recurrent bacterial peritonitis has been put forward as the main contributory factor (Schmidt & Blumenkrantz, 1981; Ing & Dangirdas, 1984), but not all patients with SP have recurrent peritoneal infection. Further factors possibly involved may include acetate containing dialysate solutions (Rottembourg et al, 1983), accidental introduction of antiseptic chlorhexidene into the peritoneal cavity (Junor et al, 1985), and the peritoneal catheter itself (Mion & Boen, 1965).

When an abdominal mass is palpated or suspected in patients maintained on CAPD, ultrasound aids in displaying its relation to adjacent viscera and its structure. For a confident ultrasonic diagnosis of an intraperitoneal pseudocyst, it is important to identify the peritoneal catheter within the pseudocyst. Early diagnosis can be achieved this way. The features of SP using ultrasound or computed tomography (Hollman et al, 1988; Korzets et al, 1988), include intraperitoneal echogenic strands, loculated ascites, abnormal small bowel peristalsis and a thickened peritoneal membrane.

In conclusion, prompt ultrasound examination allows early and confident diagnosis of pseudocyst as a complication of CAPD. This form of localized disease probably carries a better prognosis than the unrelenting encapsulating SP.

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Case reports

Spinal intradural hydatid cyst in a child

By Okan Akhan MD, Alp Dinçer MD, Işıl Saatçi MD, Nadir Gülekon MD and Aytekin Besim MD

Department of Radiology, Hacettepe University School of Medicine, Ankara, Turkey 06100

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Keywords: Echinococcosis, Paraplegia, Intradural cyst

Hydatid disease is an infestation by the larval stages of *Echinococcus granulosus*. In man, the liver and lungs are the organs most frequently involved. In the spinal column, hydatid disease usually begins in the vertebral body. Extension into the spinal canal results in spinal cord compression. Intradural hydatid cyst is extremely rare compared with the other types of spinal hydatid lesions (Rayport et al, 1964; Ley & Marti, 1970; Pamir et al, 1984).

Case report

A 6-year-old boy was admitted to hospital because of progressive paraplegia, which had started 2 months previously. He was said to have lost bladder and bowel control in the last few weeks. Physical examination revealed marked reduction in the motor power of the lower limbs. There was bilateral clonus, a positive Babinski's sign and hyperactivity of the deep tendon reflexes at the lower extremities. The chest radiograph showed multiple pulmonary opacities which were shown on thoracic sonography to be cystic in nature, compatible with hydatid cysts. Abdominal ultrasound revealed multiple anechoic cysts with double contours which were suggestive of hydatid disease. A myelogram demonstrated an intradural, extramedullary mass between the levels T9 to T11; and an immediate subsequent computed tomography (CT) scan of the region revealed an intradural cystic lesion. Immunologic studies were positive for *Echinococcus granulosus*. The erythrocyte sedimentation rate was 80 mm/h and the complete blood count showed an eosinophilia of 8%. On the basis of these radiographic, sonographic and immunological findings a diagnosis of hydatidosis was made, and treatment with Mebendazole (50 mg/Kg orally) was begun. In order to relieve the spinal cord compression, laminectomy was performed between the levels of T9 and L1. The dura mater was distended between T10 and T11, where the spinal cord was compressed and displaced to the left by a cyst with firm adhesions to the dura mater. The dimensions of the cyst were 3 × 2 × 1 cm. The dura mater and the cyst were excised. The histopathologic findings confirm the diagnosis.

Discussion

Hydatid disease due to *Echinococcus granulosus* are found in bone in 0.5% to 2% of all cases. Involvement of the vertebral column occurs in about one-half of the osseous cases because of porto-vertebral shunting (Rayport et al, 1964; Apt et al, 1976). Spinal hydatid disease may present with paraplegia or nerve root compression. The spinal hydatid lesions causing paraplegia are classified into five major groups (Braithwaite & Lees, 1981).

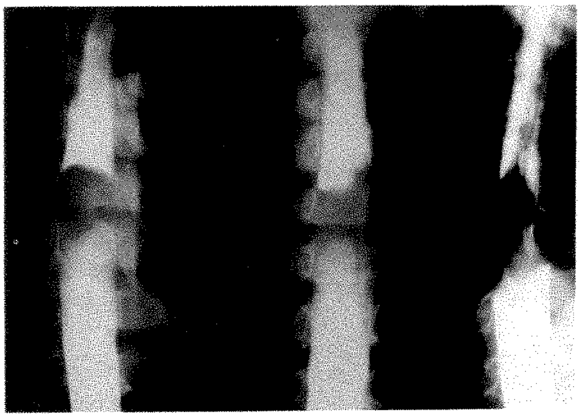

Figure 1. Lateral and both oblique views obtained by iohexol myelography show a rounded intradural mass between the levels of T9–T11 which has compressed the spinal cord to the left. There are no osseous changes.

1. Primary intramedullary cyst
2. Intradural extramedullary hydatid cyst
3. Extradural intraspinal hydatid cyst
4. Hydatid disease of the vertebra
5. Paravertebral hydatid disease

In 1970, Ley and Marti reported an intramedullary hydatid cyst, but, to our knowledge, there are no other references to such cysts. Primary extradural intraspinal hydatid cysts have been reported before, but usually they are considered to arise from an undetected bony focus (Rayport et al, 1964; Pamir et al, 1984). Paraplegia in hydatid disease is usually due to paravertebral hydatid disease or hydatid disease of the vertebra which are not easily differentiated.

Primary intradural hydatid cysts are rare and are almost always single. Multiple intradural cysts may develop secondary to rupture and dissemination from an intracranial cyst (Rayport et al, 1964). Being usually located in the dorsal region, primary intradural cysts may lead to rapid spinal cord compression. However, the prognosis is excellent after operation and recurrence is rare.

In 1967, Acquaviva et al reviewed eight cases of extramedullary subarachnoidal hydatid cysts, Carrea

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Address correspondence to: Dr Alp Dinçer, Hacettepe Tıp Fakültesi Radyoloji Anabilim Dalı, Ankara, Turkey 06100.

and Murphy reported another case in 1964, and there have been several reports of intradural hydatid cysts since 1967 (Karvounis, 1977; Bettaieb et al, 1978; Sharma et al, 1981; Pamir et al, 1984).

Our case is of interest because this patient is the youngest of all reported cases. Furthermore, our report is the first CT demonstration of an intradural hydatid cyst.

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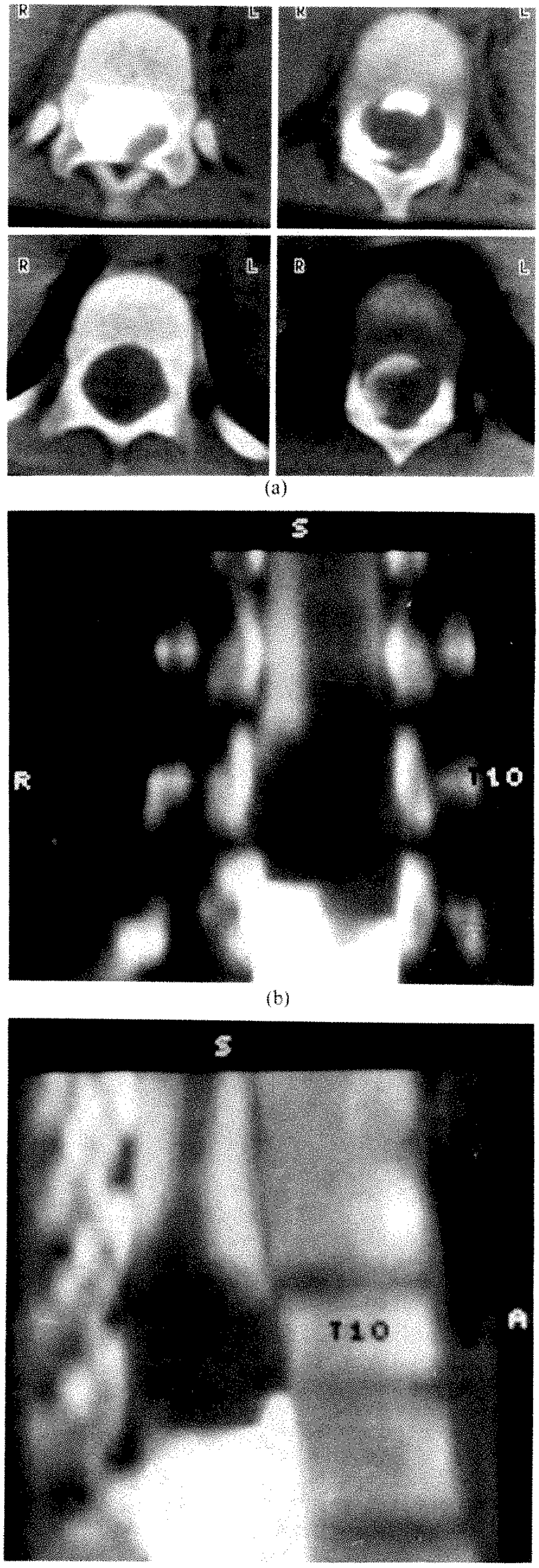

(a)

(b)

(c)

Figure 2. The computed myelograms reveal an intradural unilocular cystic lesion having a CT density between 25 and 50 H. Daughter cysts can not be seen within the cyst.

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Case reports

Metallic staples refluxing to the upper urinary tract: a source of renal calculi in patients with ileal conduit urinary diversion

By P. McCarthy, MRCPI, FRCR, L. Cheung, MD, *P. Hanno, MD and H. M. Pollack, MD

Departments of Radiology and *Surgery Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104, USA

(Received June 1990)

Keywords: Ileal conduit, Surgical staples, Calculus, Obstruction, Reflux

Surgical stapling devices to close the proximal end of the isolated loop of an ileal urinary conduit have been used since the early 1970s (Assadnia et al, 1972). However, the occasional development of calculi forming around the metal staples has deterred uniform acceptance of this technique in spite of its advantages of speed and decreased post-operative morbidity (Assadnia et al, 1972; Bergman et al, 1978).

We describe two patients who presented to this hospital in recent months, in whom surgical staples migrated proximally into the renal pelvis, becoming the nidus for stone formation in one of the patients.

Case reports

Case 1

A 62-year-old black woman with congenital syringomyelia had had a uretero-ileal diversion for neuropathic bladder 3 years previously. She presented for a routine follow-up intravenous urogram (IVU). Plain abdominal radiographs revealed several metallic surgical staples projected over the right renal outline. Plain tomography confirmed that the sutures were in the kidney (Fig. 1) and they were obscured by contrast during the subsequent IVU, confirming their location within the renal collecting system. The patient was asymptomatic and it was decided to manage her expectantly.

Case 2

A 65-year-old white woman had an ileal loop diversion after symptomatic failure of augmentation cystoplasty for severe interstitial cystitis. She had presented for a routine annual IVU 1 year previously and was discovered to have a single surgical staple probably in a left lower pole caylx. One year later, her plain abdominal radiograph showed a 1 cm calculus around a staple in the renal pelvis and the original lower pole staple had a suggestion of some calcification around it (Fig. 2). In addition, the kidney had shrunk in length from 11 cm to 8 cm and there was delay in the excretion of contrast agent (Fig. 3). The ureter had become markedly distended down to the level of the anastomosis.

The larger stone was treated with extracorporeal shock wave lithotripsy (ESWL) and in spite of the narrowed uretero-ileal anastamosis, both the stone fragments and the staples passed satisfactorily. The staple in the lower pole calyx, however, remainded. Analysis of the stone fragments showed that they were primarily made up of triple phosphates. Again, the patient was asymptomatic with respect to the stones. A loopogram was not performed in either case.

Address correspondence to Dr P. McCarthy.

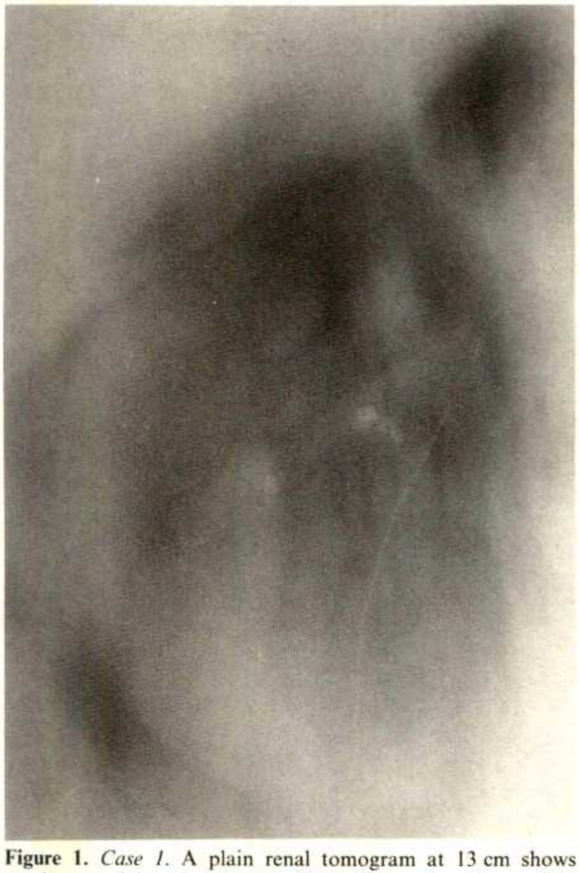

Figure 1. *Case 1.* A plain renal tomogram at 13 cm shows staple material to be clearly within the renal outline, which IVU showed to be in the collecting system.

Discussion

It has long been known that contract of urine with non-absorbable suture material invites the possibility of stone formation in ileal conduits, as well as in other structures (Assadnia et al, 1972). Because of this some of the original users of stapling devices advised that the instruments had no place in urologic operations (Assadnia et al, 1972; Bergman et al, 1978). More recent evaluations have been more sanguine (Karamcheti et al, 1978; Brenner & Johnson, 1985), but most authors acknowledge an incidence of approximately 3–7% for

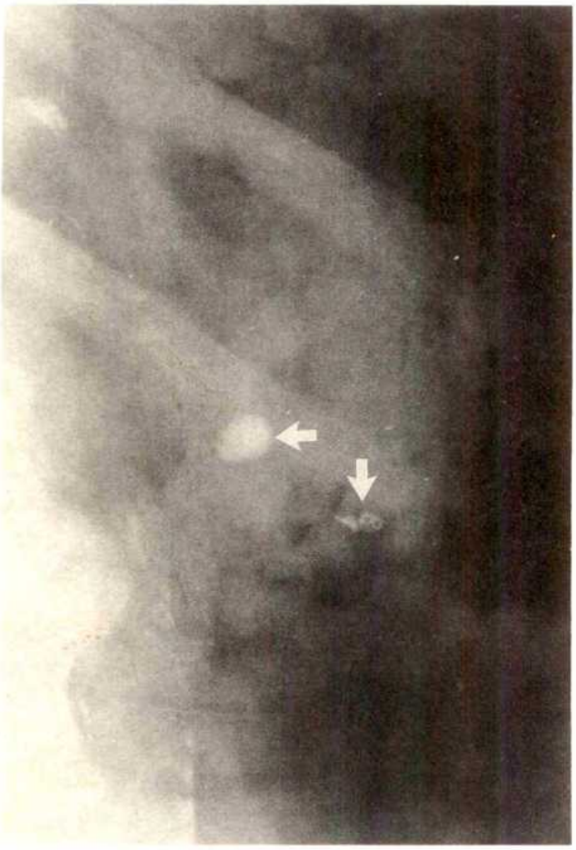

Figure 2. *Case 2.* Plain film shows a 1 cm calculus around a staple in the left kidney and a small questionable area of calcification around the staple in the lower pole.

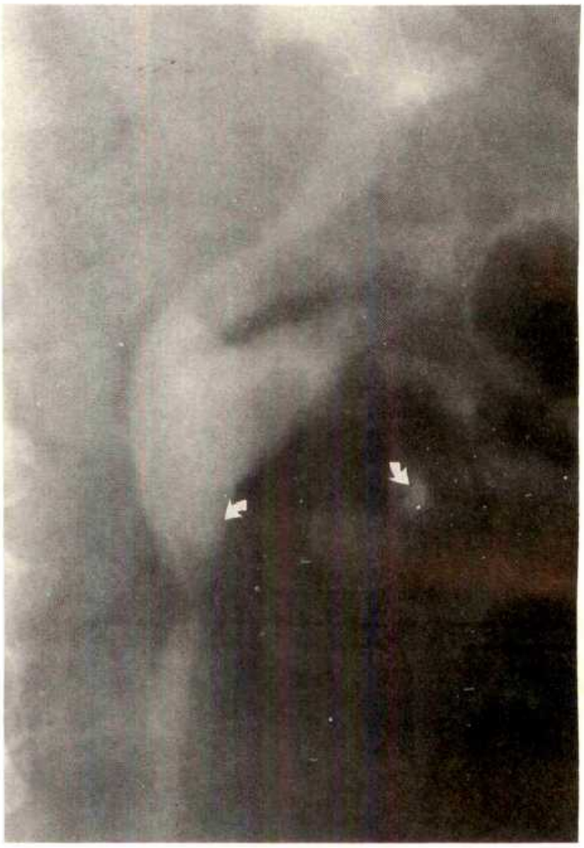

Figure 3. *Case 2.* IVU shows delayed excretion from a shrunken left kidney and the calculi lying in the lower renal pole, and in the region of the uretero–pelvic junction.

calculi forming within urinary conduits where metal staples have been used to close the proximal end of the loop (Brenner & Johnson, 1985). These stones usually form within the first two post-operative years (Brenner & Johnson, 1985). The risk of stone formation can be lessened, if not eliminated by excising the stapled proximal end of the loop and refashioning the anastomosis by hand (Heney et al, 1978; Myers et al, 1982). The recent availability of absorbable staples will probably also prove effective (Wheeless, 1984).

Since most uretero-ileal anastomoses are freely refluxing (Koehler & Bowles, 1966) and in view of the well known ability of non-absorbable materials to migrate through tissues (Trevino et al, 1979) it is surprising that more reports of staples and staple-related calculi in the upper urinary tracts of diverted patients have not appeared. One such case was recorded (Webster et al, 1987) but we are unaware of any others.

Metallic staples used for gastrointestinal anastomoses are quite small and while they are radio-opaque, their diminutive nature makes it difficult to detect them when they are located out of their usual positions *e.g.* projected over the kidneys. Failure to recognize the staples or to appreciate that they are, in an aberrant location probably accounts for the fact that other similar cases have not been reported; in all likelihood they are simply overlooked. Unfortunately even a tiny piece of metal can serve as a nidus for a urinary calculus or as a source for urinary tract infection. It is therefore important that radiologists be aware of the ability of ileal conduit sutures to reflux in to the upper urinary tract. A concerted search for such foreign bodies in diverted patients with persistent or recurrent urinary tract infection may well be rewarded by the disclosure of such minute, meandering foreign bodies, thus pinpointing the real cause of the symptoms, and perhaps preventing inappropriate diagnostic and therapeutic measures.

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Diffuse retroperitoneal amyloidosis: further radiological observations

By Ralph Posner, MBChB, FFRAD(D)SA, Avigdor M. Saks, MBChB, FFRAD(D)SA and *Gladwyn Leiman, MBBCh, FIAC

Department of Radiology, Hillbrow Hospital, University of the Witwatersrand and *Department of Anatomical Pathology, School of Pathology, South African Institute of Medical Research, University of the Witwatersrand, Johannesburg, South Africa

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Keywords: Amyloidoisis, Retroperitoneum, Retroperitoneal ultrasound, Retroperitoneal computed tomography

Amyloidosis is characterized by deposition of insoluble extracellular protein material, which may be primary (idiopathic), or secondary (due to chronic disease, especially chronic infection and neoplasms). It occurs in 6–15% of patients with multiple myeloma. In retroperitoneal amyloidosis the protein deposits usually show two distinct patterns: nodal (Takebayashi et al, 1984) or diffuse (Glynn et al, 1989). The computerized tomographic (CT) appearance of diffuse retroperitoneal amyloidosis has previously been reported (Glynn et al, 1989) as a diffuse, non-enhancing thickening of the entire retroperitoneum. The perinephric fat was not involved.

We report a further case of diffuse retroperitoneal amyloidosis and document illustrative sonographic features correlated with CT.

Case report

A 46-year-old male was admitted with a 10-month history of increasing abdominal girth, fatigue and dysarthria. On physical examination a distended doughy abdomen, general lymphadenopathy, enlarged salivary glands and macroglossia were noted. Two years previously an IgG myeloma was diagnosed following a bone marrow aspirate. Laboratory studies showed: haemoglobin, 8.3 g/dL; mean corpuscular volume, 86.4 fl; white blood cell count, 4300/mm^3; urea, 9.7 mmol/l; creatinine, 130 mmol/l; raised α2-globulin; positive Bence–Jones protein.

Ultrasound of the abdomen and pelvis showed solid encasement of retroperitoneal vasculature and viscera by a homogenous infiltrate of medium level echoes. The infiltrate extended into the mesentery, involved the perinephric fat and anterior and posterior pararenal spaces. There was an extensive retroperitoneal infiltrate in the pelvis. The diffuse involvement of the retroperitoneal tissue enhanced the definition of the abdominal vasculature on sonography (Fig. 1). The vessels were not compressed and maintained their normal calibre. No discrete nodes were present.

A CT scan was performed without intravenous contrast medium because of severe impairment of renal function. Almost total loss of definition of the retroperitoneum was noted on CT (Fig. 2). A diffuse homogenous soft tissue infiltrate caused solid encasement of the pancreas, inferior vena cava, aorta and kidneys, and extended into the mesentery and pelvis. The perinephric fat and pararenal spaces were ill-defined as a result of infiltration.

A percutaneous fine needle aspiration of the retroperitoneum, using a 22 gauge needle, was performed. The aspirate consisted of irregular fragments of eosinophilic amorphous material which, when stained by the Congo red technique, displayed the apple-green birefringence characteristic of amyloid (Fig. 3). Amyloidosis was also demonstrated on rectal biopsy.

Discussion

Amyloidosis is diagnosed in local or systemic form in less than 0.5% of hospitalized patients (Scott et al,

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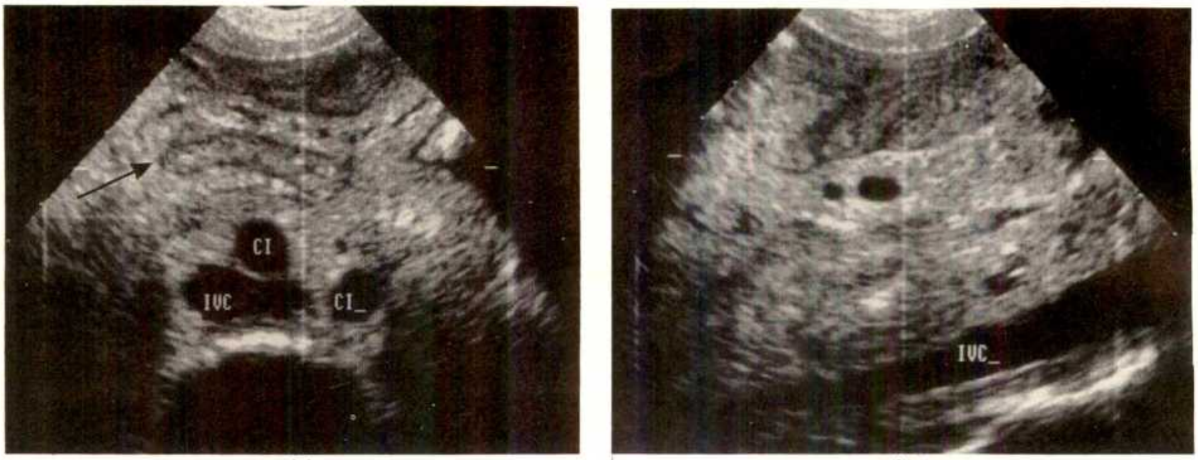
Please address requests for reprints to R. Posner, Department of Radiology, University of the Witwatersrand, Medical School, York Road, Parktown, Johannesburg 2193, South Africa.



(a) (b)

Figure 1. (a) Ultrasound scan, transverse view below bifurcation of aorta. Diffuse medium level echoes encasing and accentuating vasculature. Note the thickened bowel wall (arrow) and absence of discrete nodes. (CI: common ilias arteries; IVC: inferior vena cava.) (b) Ultrasound scan, longitudinal view. Soft tissue infiltrate enveloping retroperitoneal viscera.

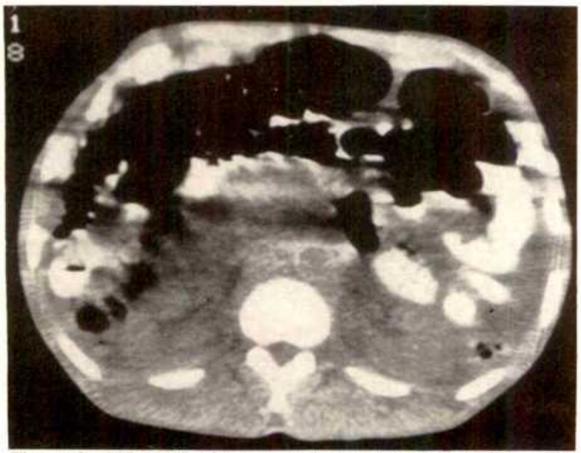
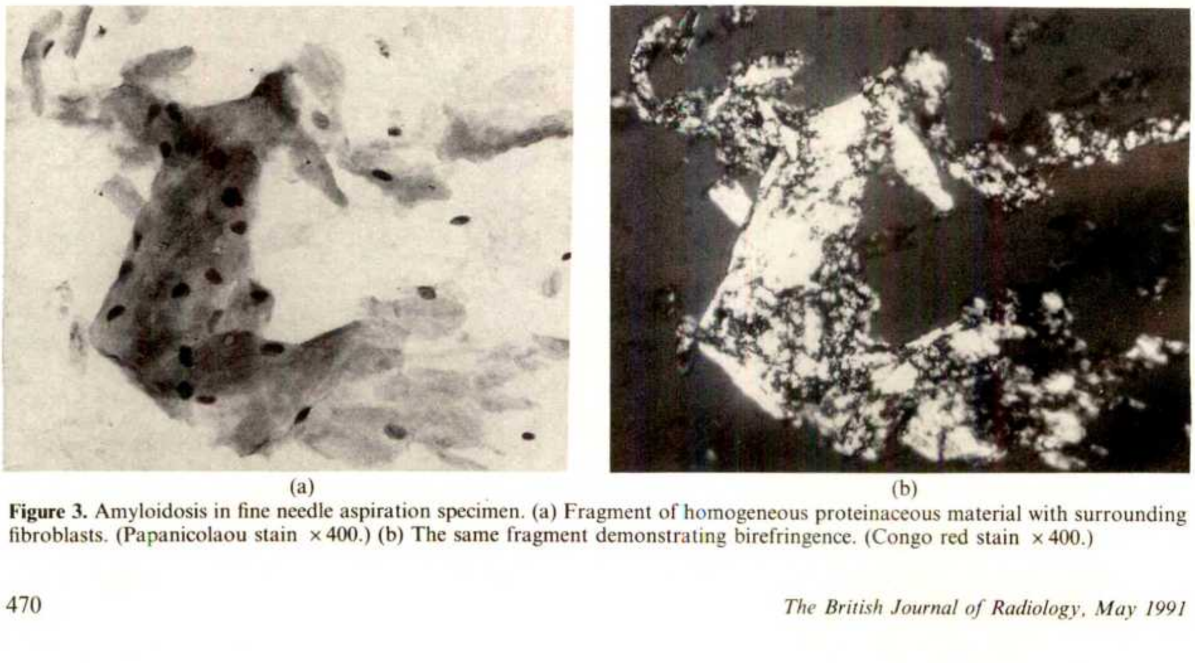


Figure 2. Axial CT of lower abdomen showing diffuse retroperitoneal amyloidosis with loss of perinephric fat planes.

1986). It has been associated with multiple myeloma and stimulation of the immune system by chronic infections, malignancy and rheumatoid arthritis (Kimball, 1961). The amyloidosis in the current case was associated with multiple myeloma.

Gastrointestinal tract involvement by amyloidosis is common, occurring in 70% of patients with primary systemic amyloid and 55.5% of patients with reactive secondary amyloidosis (Allen et al, 1985). Amyloid deposition is variable, but is commonly found in and around blood vessels, and infiltrating the viscera and bowel.

There is sparse documentation of the sonographic manifestations of diffuse retroperitoneal amyloidosis when no discrete nodal pattern could be identified.



(a) (b)

Figure 3. Amyloidosis in fine needle aspiration specimen. (a) Fragment of homogeneous proteinaceous material with surrounding fibroblasts. (Papanicolaou stain ×400.) (b) The same fragment demonstrating birefringence. (Congo red stain ×400.)

Glynn et al (1989) reported a case of diffuse retroperitoneal amyloidosis and recorded the CT features. Takebayashi et al (1984) documented the discrete echo-poor sonographic appearance of amyloidosis involving retroperitoneal nodes. In this patient, both ultrasound and CT showed diffuse amyloid infiltration of the retroperitoneum which also involved the perinephric fat, hitherto not described.

The differential diagnosis of a solid infiltrative retroperitoneal echo pattern includes haemorrhage, lymphoma, desmoplastic tumours and retroperitoneal fibrosis (Barneth & Morley, 1985).

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Percutaneous nephrostomy to relieve renal tract obstruction in pregnancy

By *M. Trewhella, FRCR, †B. Reid, MB BS, †A. Gillespie, FRCOG and §D. Jones, FRCS

Department of *Radiology, †Obstetrics and Gynaecology, and §Surgery, The Princess of Wales Royal Air Force Hospital, Ely, Cambridgeshire, UK

(*Received May 1990 and in revised form October 1990*)

Keywords: Percutaneous nephrostomy, Renal tract obstruction, Pregnancy

Dilatation of the renal tract in pregnancy is a common event (Peake et al, 1983). Whilst frequently asymptomatic, the distension can be associated with considerable pain, the acute presentation of which may be attributed to other surgical or obstetric emergencies such as appendicitis or placental separation (Anteby et al, 1975). Renal tract obstruction may also occur in pregnancy, and failure to recognize it may lead to rupture of the urinary tract and loss of the kidney (Meyers et al, 1985).

We present a case in which such a renal tract obstruction was relieved percutaneously. Whilst percutaneous nephrostomy is a commonly practised technique, its use in pregnancy has not been reported previously.

Case report

A 27-year-old multigravida who was 25 weeks pregnant was referred with a 2-day history of right loin pain and frequency. Urinary analysis showed microscopic haematuria and proteinuria. A previous pregnancy had been uneventful, and her uterine ultrasound scan at 16 weeks' gestation was normal. On admission, she was apyrexial with a normal pulse rate and blood pressure. On examination, there was tenderness in the right iliac fossa. Cardiotochography was normal. Biochemical and haematological indices were normal: urea 2.9 mmol/l, creatinine 85 mmol/l. An ultrasound scan showed a right hydronephrosis and hydroureter. The left renal tract was normal. No evidence of placental separation or fetal abnormality was seen. A ^{131}I hippuran probe renogram showed reduced right renal function (37%) and a rising right excretion curve (Fig. 1). In view of the right renal obstruction and decreased function, a percutaneous nephrostomy was per-

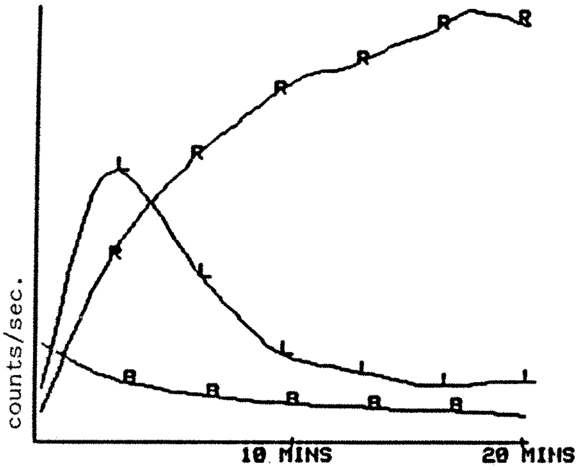

Figure 1. Excretion curves of ^{131}I hippuran isotope study at 25 weeks gestation (corrected for background).

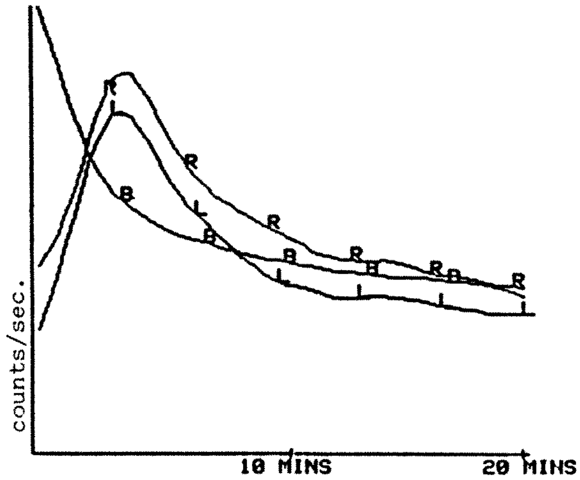

Figure 2. Excretion curves of ^{99m}Tc DTPA isotope study, 6 weeks after delivery (corrected for background).

formed with a pigtail catheter being inserted into one of the lower pole calyces. This led to immediate relief of the pain. The patient learned nephrostomy care and was discharged a week later on prophylactic trimethoprim 100 mg daily. She was reviewed weekly, and on three occasions reduced urine output from the catheter was restored by gentle flushing with normal saline. A coliform infection at 37 weeks' gestation was treated with ampicillin. At 38 weeks, labour commenced, and a healthy 3125 g girl was delivered vaginally. An antegrade study via the nephrostomy and a renal ultrasound scan performed 2 days after delivery showed less dilatation than during pregnancy and no evidence of ureteric obstruction. The nephrostomy catheter was clamped for 24 hours and no problems arose. It was then removed, and mother and baby were discharged on the sixth post-natal day. Six weeks after delivery, the patient remained asymptomatic, and a ^{99m}Tc DTPA renogram showed equal renal function on both sides with no evidence of renal obstruction (Fig. 2).

Discussion

The possibility of obstruction rather than physiological ureteric dilatation of pregnancy was raised in this case by the combination of hydronephrosis and ipsilateral loin pain. It was confirmed by a probe ^{131}I hippuran isotope study, chosen in this instance rather than the more widely available ^{99m}Tc DTPA because the fetal radiation dose is much lower: 0.016 mGy for 1 MBq ^{131}I hippuran; 1.5 mGy for 200 MBq ^{99m}Tc DTPA.

Retrograde catheterization for the relief of renal tract obstruction has been described in such cases (Nielsen & Rasmussen, 1988), but it was felt that the percutaneous approach had the advantage of avoiding the need for a general anaesthetic and the potentially hazardous attempted bypass of an obstructed ureter with a stent. To be successful, however, this technique does require that the patient can satisfactorily manage a nephrostomy as an outpatient.

Acknowledgments

We would like to thank Dr E. P. Wraight of the Department of Nuclear Medicine, Addenbrooke's Hospital, Cambridge for performing the isotope studies and discussing the results with us.

We would like to thank the Director General of Medical Services (RAF) for his permission to present this case report.

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Case of the month

A pearl of wisdom

By J. Rawlinson, MA, FRCS, FRCR, C. L. Coblentz, MD, FRCPC and S. Franic, MD, FRCPC

Department of Radiology, McMaster University Medical Centre, 1200 Main Street West, Hamilton L8N 3Z5, Ontario, Canada

(*Received March 1990*)

An 8-year-old girl presented with progressive unsteadiness on her feet over a 2-year period. She was otherwise fit and well. No neurological deficit was found on examination, but movements of the lumbar spine were reduced. Conventional radiographs of the lumbar spine, myelogram and computed tomography (CT) myelographic findings are demonstrated in Figs 1–3, respectively.

What is your differential diagnosis? What further information would you seek to clarify the diagnosis?

Address for correspondence: Dr J. Rawlinson, Fellow in Radiology, Department of Radiology, McMaster University Medical Centre, 1200 Main Street West, Hamilton L8N 3Z5, Ontario, Canada.

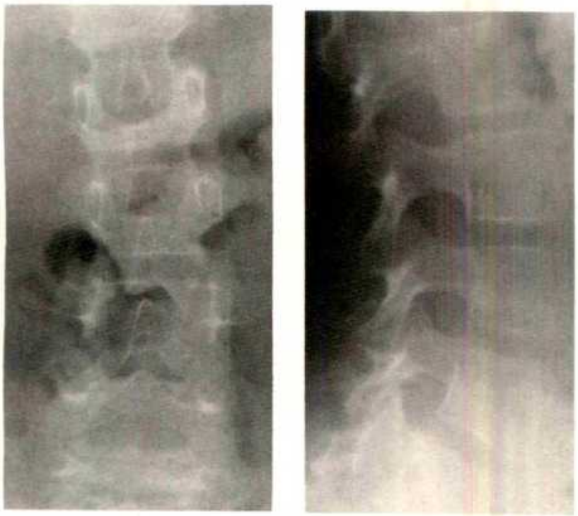
(a) (b)

Figure 1. (a) Anteroposterior and (b) lateral conventional radiographs of the lumbar spine.

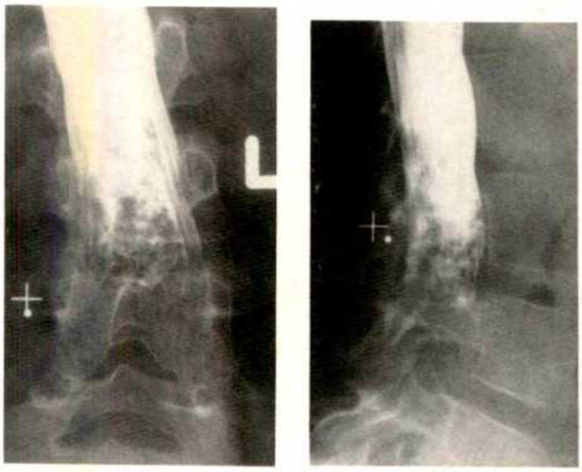
(a) (b)

Figure 2. Myelogram: (a) anteroposterior and (b) lateral views of the lumbar region.

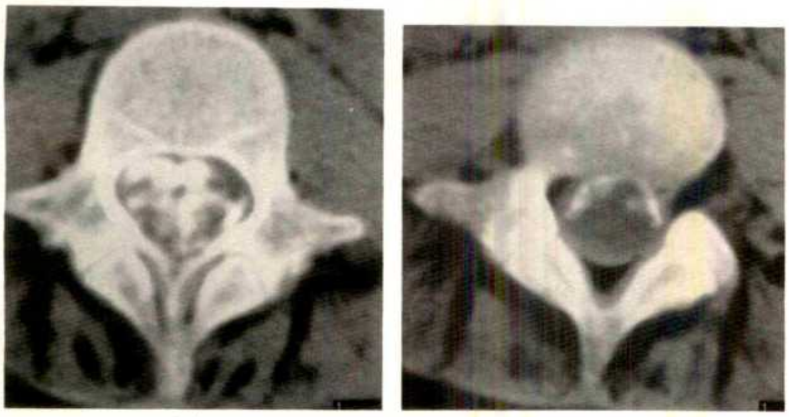
(a) (b)

Figure 3. Post-myelography CT: axial sections (a) through the body of L3 and (b) at the level of the L3/4 disc.

The plain radiographs of the lumbar spine show a scoliosis concave to the right and subtle scalloping of the posterior aspects of the lumbar vertebral bodies 3–5. On the anteroposterior view there is some flattening of the medial side of both L4 pedicles. There is no evidence of bone destruction, disc space narrowing or expansion of the exit foramina.

The myelogram demonstrates an intradural mass composed of conglomerate nodules embedded within the cauda equina. This mass has expanded the theca and obstructed the flow of contrast in a caudal direction from the level of L3. Post-myelography CT shows the intradural lesion intimately related to the cauda equina. The mass is low in density and cannot be easily differentiated from the nerve roots.

An intradural "pearly grey" mass was found at surgery. This was loosely adherent to the nerve roots of the cauda equina from which it was easily peeled. Histological examination of the excised tissue showed abundant keratin composed of stratified squamous epithelium with characteristic features of an epidermoid tumour. Following surgery the patient made a complete recovery.

Discussion

The differential diagnosis of an intradural mass at this site in childhood includes ependymoma of the filum terminale, lipoma, neurofibroma, metastases (*e.g.* medulloblastoma, neuroblastoma), dermoid/epidermoid tumour and teratoma; meningiomas may also rarely occur in childhood (Peacock & Lazareff, 1986). The plain radiographic findings and the length of the history suggest a slow growing, relatively benign lesion. Lipomas and dermoid/epidermoid tumours are usually associated with spinal dysraphism, for which there is no evidence here; neurofibromas commonly involve the exit foramina and are associated with other stigmata of neurofibromatosis.

Epidermoid or "pearly" tumours of the central nervous system are rare and usually found in the posterior fossa; they are even less common in the spinal canal where they tend to occur in the lumbosacral region. In a review of 90 intraspinal epidermoid tumours (Manno et al, 1962), all were located in the lumbar region and most were in children. It is notable that 39 (43%) of these patients had been subjected to lumbar puncture in periods ranging from 6 months to 10 years prior to their presentation.

Lumbar punctures in children, particularly infants, are sometimes performed using a "butterfly" infusion needle (Halcrow et al, 1985; Ersback & Hobolth, 1988). Such unstiletted needles may collect a core of epithelial tissue during their passage through the skin (Gibson & Norris, 1958); furthermore, this tissue can implant and grow within the theca (Van Gilder & Schwartz, 1967). There is good presumptive evidence, therefore, that intraspinal epidermoid tumours may be a late complication of lumbar puncture. Normal myelograms prior to lumbar puncture in at least four of the reported cases support the hypothesis of iatrogenic implantation of epithelial cells.

The relevant information which should be sought to clarify the diagnosis is a history of lumbar puncture. Our patient had undergone two lumbar punctures at the age of 4 months to investigate a neurological reaction to metoclopramide, administered for vomiting. A full recovery was made and she was subsequently well until becoming unsteady on her feet at the age of 7 years.

While the incidence of iatrogenic intraspinal epidermoid tumours appears to be declining (Visciani et al, 1989), two cases have recently been reported (Ersbak & Hobolth, 1988; Visciani et al, 1989); also, a survey in 1985 (Halcrow et al, 1985) showed that 32% of paediatricians routinely use an unstiletted needle for lumbar puncture in neonates and small children. Sporadic cases are therefore likely to occur in the future and may be encountered by those involved in neuroradiology.

Keywords: Epidermal cyst, Cauda equina, Iatrogenic disease

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Proceedings of the British Institute of Radiology

Practical issues in breast cancer screening

Abstracts presented at a meeting organized by the BIR Diagnostic Methods Committee, held at the Scientific Societies Lecture Theatre, New Burlington Place, Piccadilly, London W1 on Thursday 17 January 1991

Chairman: G. H. Whitehouse
Choosing films, screens and cassettes, by J. Law
Quality assurance and the breast screening programme, by N. M. Perry
Uptake in the breast screening programme, by G. J. Bickler
Evaluation of radiologist performance in reading mammograms, by A. G. Gale and A. R. M. Wilson

Chairman: A. K. Tucker
Interval Cancers, by C. Rubin
The assessment of abnormalities detected by mammographic screening, by M. J. Michell
Stereotactic FNA, by F. E. White
The role of the primary care team in breast cancer screening, by J. Austoker

Chairman: D. L. Asbury
Breast screening — the European scene, by A. K. Tucker
UKCCCR research into aspects of breast screening, by J. Chamberlain

Choosing films, screens and cassettes

J. Law
Department of Medical Physics and Medical Engineering, Western General Hospital, Edinburgh, EH4 2XU

This presentation will give an outline of methods of choosing equipment but will not attempt detailed reviews of named models or types, or of the products of named manufacturers. Most attention will be given to films, screens and cassettes, but X-ray sets and film processors will also be briefly considered. Examples of practical problems will be given. These are drawn from experience in several series of comparisons of films and screens already reported in the BJR (eg Vol. 63, pp. 128-131, February 1990), from evaluation of certain X-ray sets for the Department of Health and from experience in choosing equipment and monitoring its subsequent performance in the breast screening programme in Scotland.

Quality assurance in the national breast screening programme

N. M. Perry
Quality Assurance Reference Centre, North East Thames Health Authority, St Bartholomew's Hospital, Gloucester House Extension, 1st Floor, Bartholomew Close, West Smithfield, London, EC1A 7ED

The benefits of breast screening will be best delivered by a service incorporating quality at all levels. The Forrest Report recognized the need for quality assurance (QA) to be an integral part of the National Programme. The Department of Health - HC(89)6 - recommended regional health authorities to nominate a QA manager and establish a QA reference centre by March 1990. Other recommendations included staff training and development of QA manuals locally. Quality control mechanisms exist at local levels:

QA maintains quality across the service. The essence of QA is the setting of minimum standards and the continual pursuit towards excellence (Muir Gray). Major domains of QA include acceptability, mammography, pathology, information systems, treatment and management. Key elements include setting up the organization and activities of the service (structure and process) and documenting results (outcome). Process and outcome objectives are described in the Quality Assurance Guidelines for Mammography (the Pritchard Report), and outcome objectives have recently been refined in the light of experience by the Royal College of Radiologists. Regional and national networks exist with relevant professional and technical co-ordinators to ensure passage and feedback of information and to deal with problems as they arise. The national network is headed by the Department of Health Advisory Committee, liaising with the National Co-ordinators' Group, the QA Managers' Group and the Information and Evaluation Group. These in turn communicate with the relevant professional sub-groups and colleges. Trent is the co-ordinating region for the National Programme. It remains to be seen whether a tangible quality marker such as the British Standards Institute BS 5750 is applicable to breast screening. The concept of Total Quality Management, i.e. a service focused on its consumers (in this case women), developing a quality culture within staff and measurement of performance with feedback has great relevance to the National Programme.

Uptake in the breast screening programme

G. Bickler
Consultant in Public Health Medicine, Camberwell Health Authority, Bessemer Road, London, SE5 9RS

In the Forrest report it was argued that a 70% acceptance for breast cancer screening in the national programme would be a reasonable and achievable target. The latest national data show that so far we have all but achieved this, but that there are still a number of important issues to consider. First, we have still to start to use standardized definitions of acceptance, and the databases from which they are calculated are often highly inaccurate. Anyway, population coverage is arguably a more important measure than acceptance. Secondly, there have been a number of studies which have shown that acceptance varies with demographic factors, medical history, health service use, access to screening and women's beliefs and attitudes. We must be clear about the implications of their findings and act upon them. If we do not, then not only will response rates fall but some groups of women such as those from lower income brackets and older women will be particularly disadvantaged. The major areas of concern are that:

(a) health education messages should be tailored to individual needs and should address commonly held negative beliefs about breast cancer while giving positive messages about the value of screening;

(b) the role of the primary care team, and in particular GPs, should be acknowledged and developed as it is likely that their attitudes are a major determinant of participation.

Finally, in studies in Sweden, the USA and Edinburgh, the acceptance rate decreased with each screening round, so it is vital that we identify ways of minimizing or preventing this phenomenon. The research on uptake is relevant to this but specific further research is needed.

Evaluation of radiologist performance in reading mammograms

A. G. Gale and *A. R. M. Wilson
Academic Department of Radiology, University Hospital, Nottingham, NG7 2UH and **Department of Radiology, University Hospital, Nottingham, NG7 2UH*

Highest possible standards of performance in mammographic screen reading are fundamental to the success of the National Health Service Breast Screening Programme (NHSBSP). To train radiologists in the skills required, formal training programmes have been incorporated into the NHSBSP from the outset. The nationally implemented quality assurance programme currently only measures crude outcomes. Recognizing the need to supplement the National Quality Assurance Initiative the Royal College of Radiologists and the Department of Health have commissioned a mammography reading task which is designed to provide radiologists with rapid and accurate measurement of their screen reading performance. Radiologist performance is measured on a standard file reading task comprising a set of recent screening mammograms of known pathology. Individual and collective performance can be monitored and compared with an accepted norm. Tailored revision and advice can be offered where significant variance is identified. Each radiologist is given feedback on their own performance together with the anonymous overall data of others, allowing them to see how they compare with the group standards. Regular re-reading of the task will also enable assessment of how performance varies with experience. Various performance indices are recorded including signal detection theory measures of d' Beta and Az for both detection and recognition ability. After piloting the methodology at the Nottingham Breast Screening Training Centre, an initial trial is in progress in the Trent, East Anglian and Northern Regions, prior to full national implementation. The background to the study, the evolution of the investigative methodology and present up-to-date data from the trial are discussed.

Interval cancers

C. M. E. Rubin
Department of Radiology, Southampton General Hospital, Tremona Road, Shirley, Southampton, Hampshire, SO9 4XY

Twenty cancers have been identified in the screened population in Wessex during the interval between screening episodes. These have occurred within a maximum interval of 2 years 4 months since the first unit started screening in June 1988. The overall incidence is 4 per 10,000 women screened. 55% presented within the first year and 45% in the second year after screening. 55% were regarded as true interval cancers by two radiologists from different centres reviewing the screening films together with a matched control. Review of the mammograms at presentation showed that three of these were mammographically occult because of unusual position and not visible on the oblique view. In 45% of cases there was evidence of an abnormality on the screening films. The abnormalities missed were microcalcifications (33%), asymmetrical densities (33%), masses (22%) and stromal distortion (11%). Histological type, grade and tumour staging have been compared with the screen detected cancers as well as tumour staging data for women in the age group 50-64 diagnosed in 1987 before screening started. The impact of double reading on reducing interval cancer rates is shown in seven cases which were recalled for assessment after a third read. Six were potentially missed microcalcifications and one case of Paget's disease was recalled on clinical grounds. Of these cases four had in-situ disease, but three had minimally invasive tumours which may well have presented as interval cancers in the absence of double reading.

The assessment of abnormalities detected by mammographic screening

M. J. Michell
King's College Hospital, Denmark Hill, London, SE5 9RS

5-10% of women who undergo standard 45 degree oblique screening mammography will be found to have an abnormal appearance on the films which requires further assessment. This is carried out in a specialized clinic where radiological, radiographic, clinic, pathological and counselling skills are available. The main aims of the clinic are to:

(1) identify those women who have a suspicious breast lesion which warrants biopsy;

(2) identify those women who either have no significant abnormality in the breast or a definitely benign lesion, who can be positively reassured that no further action is necessary.

All women require craniocaudal views to complete the basic mammographic examination. Further radiological tests, which may include non-magnified lateral or extended craniocaudal views, localized paddle compression and magnification techniques and ultrasound, are chosen to solve specific problems and to characterize a lesion as far as possible. A clinical consultation, including physical examination of the breasts, provides the opportunity to correlate any abnormal physical findings with mammographic abnormalities and to offer appropriate counselling to both those women with and those without a significant abnormality. Fine needle aspiration cytology, now available in many centres, can be used to confirm a malignant or a benign diagnosis. Before leaving the clinic, the woman is given a clear explanation as to whether a significant abnormality is present, and if so the nature and timing of any further tests or treatment are discussed.

Stereotactic fine needle aspiration biopsy of the breast

F. E. White
Department of Radiology, Royal Liverpool Hospital, Liverpool

Stereotactic fine needle aspiration is a valuable technique in the evaluation of impalpable breast lesions. Many mass lesions can be biopsied using ultrasound guidance but this is unsuitable for microcalcification and areas of stromal deformity. Confirmation of suspected malignancy by FNA removes the need for a diagnostic surgical biopsy, allowing wide local excision to be performed at the first operation. It is useful in assessing suspected multifocal cancer or in confirming the diagnosis where surgery is contraindicated. In a screening programme, stereotactic FNA is extremely helpful in assessing indeterminate lesions or in confirming benignancy, thus avoiding surgery in many cases. Problems with needle positioning occur if XY axis centring is inaccurate. This is particularly relevant in cases of stromal deformity and loose clusters of microcalcifications. A greater yield of material is obtained if the needle is inserted to a depth below the lesion, as the needle is partially withdrawn during aspiration. When biopsying mass lesions it is often necessary to increase the depth until the mass can be felt with the needle. By injecting contrast at the site of the FNA and taking a film at 90 degrees, one can confirm that the needle has traversed the abnormal area and that the sample obtained is therefore representative. In our experience of more than 350 stereotactic FNAs, the yield of cells has been greatly improved by taking 3-4 samples at varying levels. Despite correct positioning, some lesions still tend to give poor yield of cells, e.g. hyalinized fibroadenoma, scar tissue post DXT. Since the provision of an FNA service in our unit, the numbers of surgical biopsies has fallen and our benign:malignant ratio has changed from 2:1 to 1:3.

The role of the primary care team in breast cancer screening

J. Austoker
CRC Primary Care Education Group, University of Oxford, Department of Public Health and Primary Care, 2 Polstead Road, Oxford, OX2 6TN

For the National Breast Screening Programme (NBSP) to be successful the active contribution and co-operation of primary care teams is essential. Primary care teams can help to improve the quality and acceptability of the programme, increased uptake, and provide information and counselling related to all aspects of the programme. If women are to be given accurate and appropriate information and advice, it is important for all members of the primary care team to understand the organization of the programme, the implications of a recall for further investigation, and the implications of being found to have a cancer. General practitioners, practice nurses and health visitors are also in an ideal position to discuss breast screening with non-attenders. A study of 500 practices from 13 Regional Health Authorities, Wales and Northern Ireland has looked in detail at the involvement of primary care teams in the NBSP and at practical problems being encountered in effecting this role. It has also analysed the range of enquiries being made by women, how the programme is being publicized in practices, and how practices are dealing with non-attenders. These observations have been incorporated into the NBSP education and training initiative for primary care teams.

Breast screening — the European scene

A. K. Tucker
Department of Radiology, St Bartholomew's Hospital, West Smithfield, London, EC1A 7BE

Population screening has been introduced gradually throughout Europe over the last 20 years. One of the earliest programmes started in Sweden in Gavle in the late 1960s by Dr Bengt Lundgren. Many other centres have now been established in Sweden. In Italy, a screening centre was established in 1970 which has since expanded. In Holland, centres were established in 1974 in Utrecht and in 1975 in Nijmegen. Germany and France now have established centres in several of their large cities. Belgium, Spain, Portugal, Greece and Ireland have also started projects in association with Europe Against Cancer. The UK project is as yet the only project which involves the whole country giving free screening to all women between 50 and 65 years of age who are registered with a general practitioner. Combination of the results from all the various screening programmes should ultimately give very interesting results on the various parameters of each screening programme such as number of views, age and methods of invitation.

UKCCCR research into aspects of breast screening

J. Chamberlain
Block E, Royal Marsden Hospital, Downs Road, Sutton, Surrey, SM2 5PT

Following the publication of the Forrest Report, the UKCCCR set up a Subcommittee to develop and co-ordinate research into the issues raised in Chapter 10 of the report, issues requiring further research. The Subcommittee initially took a pro-active role in establishing Working Groups to develop protocols for three priority areas: screening of women under age fifty, the optimum interval between routine screens, and an analysis of the cost-effectiveness of single view versus two-view mammography at the initial screen. These protocols were then subjected to the usual Medical Research Council peer review process, all were approved and joint funding for 5 years was obtained from the UKCCCR sponsors and the Scottish Home and Health Department. The protocols for these three studies, each of which is now in its pilot phase, will be described. The UKCCCR Breast Screening Research Subcommittee, in addition to monitoring the progress of these trials, is also trying to establish and co-ordinate research into improving the uptake of screening, and also keeps under review the status of other issues relevant to the screening programme including the psychological consequences, the potential role of tumour markers, and evidence on the natural history of breast cancer.

A report of this meeting is given in the BIR Bulletin at the back of this issue of BJR (p. B44)

BIR Bulletin

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BIR Ultrasound Pioneer Wins 1991 Japan Prize

The announcement has been made of the award of the seventh Japan prize to Dr John Wild, one of the latest (1990) recruits to the ranks of honorary membership of BIR.

John Wild took Natural Sciences Tripos at Cambridge in 1936, where he subsequently qualified in medicine in 1942 and obtained a PhD in 1971. He moved to the University of Minnesota in 1946 to practice as a surgeon and has settled in America, although remaining a British subject.

The Japan Prize is not only valuable (50 million yen, or £200,000) but carries very considerable international prestige. One of the two relevant scientific fields for this year's award was imaging techniques in medicine and the choice of Wild could not have been more fitting. In abbreviation, his citation for the prize reads as follows:

> The science and practice of ultrasonic echographic imaging was initiated simultaneously and independently by two individuals, Drs John J. Wild and Douglas Howry, in the years 1946–1950. However, in terms both of priority of publication and also in the breadth of his work, there are very strong grounds for placing Wild as the leading pioneer. Wild's original and published contributions during the 1950's included: demonstration of the existence of soft tissue echoes, development of real-time grey scale B-scan equipment, use of this for imaging soft tissue pathology, development of intracavitary imaging for bowel and prostate, objective tissue characterization, and investigation of hazards.

Wild – "The name is Wild, as in wild, wild women" – has always been a colourful character, a fact perhaps not unconnected with the abrupt termination in 1962 of his US public health service grant, which won him the following entry in the Guiness Book of Records: "A sum of $16.8 million was awarded to Dr John Wild, 58, at the Hennepin District Court, Minnesota, USA on 30 November 1972 against the Minnesota Foundation and others for defamation, bad-faith termination of a contract, interference with professional business relationship and $10.8 million in punitive damages". Not only a pioneer, but a litigant to be reckoned with!

KIT HILL

Professor C. R. Hill (left) and Dr J. Wild at the BIR 1990 Conversazione

Practical Issues in Breast Cancer Screening — 17th January 1991

A report on the meeting held at the Scientific Societies Lecture Theatre, New Burlington Place, London, organized by the BIR Diagnostic Methods Committee.

By Dr D. L. Asbury Consultant Radiologist, Withington Hospital, Manchester M20 0PT

In years to come, when asked what they were doing when the Gulf War started, approximately 150 British radiographers and radiologists will be able to say that they were attending a meeting in London on "Practical Issues in Breast Cancer Screening". This strange conjunction of events lent an air of unreality to the proceedings, but did not ultimately prevent the success of a well planned meeting.

The venue was new to many: the Scientific Societies Lecture Theatre, New Burlington Place, Piccadilly. This is a large, well ventilated, comfortable lecture theatre. There were some problems during the first session with the sound quality but this was overcome later. A less committed audience would have found the situation most convenient for the January sales in Regent Street and environs, but these paled into insignificance when compared to the attractions of the programme devised by Professor Graham Whitehouse on behalf of the BIR's Diagnostic Methods Committee.

Introducing the first session Professor Whitehouse indicated that now that many centres had been screening for 2 years, the meeting provided an opportunity to pause and take stock. As befitted an event organized by the BIR, and a programme within which teamwork is so vital, the contributors would be from multiple disciplines.

The morning session was constructed around aspects of the primary screening function, and began with a paper by Dr J. Law from the Department of Medical Physics, Edinburgh, entitled " Choosing films, screens and cassettes." In a crisp, highly relevant presentation Dr Law did not present a "best buy" catalogue but showed how we would make our choices. He stressed the importance of visiting other centres, involving engineers and physicists, carrying out objective tests, taking nothing for granted, and not being afraid to ask for replacements. His paper could, with advantage, be published by our journal or one of the Breast Screening Programme initiatives.

Dr N. M. Perry, Consultant Radiologist, with responsibility for quality assurance (Q.A.) in North East Thames Health Authority spoke next on "Q.A. in the national breast screening programme". The importance of Q.A. is attested by its inclusion as one of the six national initiatives. It covers many domains other than radiology. The possibility of applying the Kite-mark system of the British Standards Institute (BS 5750) to screening programmes was described, and there was a useful introduction to a strange new jargon: "Zero Defect Philosophy"; "Total Quality Management" etc. This is a major growth area: a potentially top-heavy committee structure has burgeoned, but the daily application of these highly commendable principles remain difficult — and as Dr Perry stressed "quality does not come cheap".

The multidisciplinary approach was continued by Dr G. J. Bickler, a Consultant in Public Health Medicine from Camberwell Health Authority whose topic was "Uptake in the breast screening programme". Although on average the Forrest figure of 70% compliance is being approached nationally, there are wide variations (39–83%). Dr Bickler reviewed some of the factors affecting uptake. He recognized the discouraging fact that many of them are not readily subject to modification. He also tackled the problem of standardized definitions of acceptance, and indicated that population coverage is arguably a more important measure. It is to be hoped that improvements can be made because compliance is likely to decrease in the incident rounds.

The morning session concluded with a joint presentation by the Nottingham team of Dr A. R. M. Wilson, Radiologist, and Dr Gale, Psychologist, on the programme for "Evaluation of radiologist performance in reading mammograms". This has been developed at the Nottingham Training Centre and will be further tested in East Anglia and Northern Regions before possible national implementation. The results of the
will be confidential and for the benefi
the individual radiologist. It was
made clear what fate will befall th
who persistently fail to meet nati
norms!

The high attendance placed s
strain on the catering and seating
rangements for lunch (not included in
basic registration fee), but the break o
hour provided a much needed oppo
nity for meeting friends and infor
exchange of views. In the lunch
there was a small display of manufac
ers' literature relating to films and scre
and one company displayed its nee
for localization and biopsy techniqu

In the first session of the aftern
attention turned to the assessment sid
screening. Dr Caroline Rubin, Cons
ant radiologist from Southampton, t
on the humbling task posed by "Inte
cancers". She clearly defined the te
used, stressed the importance of an ac
cancer intelligence unit, and gave
dence of the benefit of double readin
films. In a very well illustrated prese
tion Dr M. J. Michell from King's
lege Hospital, London, described "
assessment of abnormalities detecte
mammographic screening". Initially t
results were very poor, but with exp
ence they have transformed their p
tice. Their benign to malignant bi
ratio was 2:1 before the advent of F.
and was now 1:3.5. She gave a c
presentation of pitfalls and useful tr
of the trade. Reverting to the bro
perspective Dr Joan Austoker from
ford described "The role of the prim
care team in breast cancer screeni
This was a summary of her Nati
Training Initiative Yellow Boo
Visiting Primary Care Teams to Exp
Their Part in the Screening Program

The final session began with a p
by Dr Audrey Tucker recently ret
from St Bartholomew's Hospital, L
don, who comprehensively surveyed "
European scene". Although many cen
have been long established, Brita

remains the only truly national screening programme. The last paper of the day was given by Professor Jocelyn Chamberlain who clearly summarized the three main research studies being organized by the UKCCCR mainly viz. screening for the under 50's; one versus two view screening; and screening at intervals less than 3 years. These are being mounted at an additional cost of £5 million and in the case of the first study at least will not provide reliable results for 10 to 15 years.

With Q.A. being such a vogue topic the impact of the meeting should perhaps have been determined by a "course evaluation questionnaire". I think the meeting provided a useful review but was perhaps too didactic, with insufficient audience response. A future meeting might benefit from more controversy injected by members of the multi-disciplinary team absent from this event: a critical surgeon or hard-pressed GP.

The proceedings of this meeting
can be found on pages 475–478
of this issue of BJR.

Library News

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays and Thursdays).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

There is an agreement which allows limited use of the RSM library for reference purposes, including photocopying and searches.

Members should apply to the BIR librarian for a visitors card.

Recent additions to the library

- Boijsen, E. & Kormano, M., 1987. Iopentol. Chemistry, toxicology and pharmacology of a non-ionic contrast medium.
- Novak, R., 1988. Transformation of the female breast during compression at mammography with special reference to the importance for localization of a lesion.
- Erikson, U. & Boijsen, E., 1988 (Eds), Doctoral theses in radiology from Uppsala University Sweden.
- Plenkovich, D., 1989. Electronic scanning-slit fluorography.
- Fraser, R. G. et al, 1989. Diagnosis of diseases of the chest, Vol. 1–3.
- Merritt, T. A., Northway, W. H. & Boynton, B. R., 1988 (Eds). Bronchopulmonary dysplasia.
- Pollack, H. M., 1990 (Ed). Clinical urography, vol. 1–3.
- Scherer, E., Streffer, C. & Trott, K., 1990 (Eds). Radiation exposure and occupational risks.

RSNA 1990

Why do so many of the British radiology community visit Chicago in November every year? It can't be for the weather since Chicago is normally very cold in November and more often than not it snows and fully lives up to its "Windy City" reputation. The answer is of course RSNA which normally makes its home in the vast McCormick Place Exhibition and Conference Centre for a week at the end of November. This is the world's largest radiology conference and exhibition — a "must" for those wanting to keep abreast of the latest developments.

November 1990 was no exception, and the 24th saw over 40 000 delegates and company representatives arriving from all over the world to attend this meeting. This year's meeting was even more popular with British attendees than in previous years, although this means only about 200!

This show has increased in size every year and those who came to RSNA 90 found even more to see. For anyone attending for the first time this meeting can be quite overpowering. There were 1130 scientific lectures in 12 sub-specialities and over 500 company exhibitors with some of the stands 60 x 40 feet on two levels; there are said to be over 4 miles of aisles within the scientific and technical exhibition, so the numb feeling in the feet and legs at the end of the day can be understood. Luckily Chicago boasts a wide variety of opportunities for evening relaxation so one can recover to some extent, unless you are unwisely given to burning the midnight oil.

RSNA 1990 had a main theme: "uncommon vision". Always there is the continuing educational aspect common to USA medical conferences, and credit towards the CME requirement by attendance at the lectures and workshops is a major impetus to coming to the meeting. There were 192 refresher courses, 16 workshops and an enlarged and updated 'MRI 1990' 8-session course, together with special courses on "Clinical trials in radiation therapy" and "Emergency department radiology". There was a tremendously wide variety of topics covered by the scientific papers and poster sessions. The scientific programme has 18 parallel sessions so it is impossible for anyone to attend all the lectures that they might want to. This year the topics covered 12 well defined sub-specialities — all aspects of radiology (seven sections) with physics, nuclear medicine, ultrasound and therapeutic radiology. The poster sessions had 965 presentations and 336 "work in progress" sessions in addition to the 1130 main papers and 13 plenary sessions.

In the technical exhibition there was no dominating theme this year but it was unusual to see a stand without the ubiquitous computer in some form or other; even some of the publishers had computer databases running for their lists of technical and clinical books and journals. An innovation this year was the *info-RAD* feature which was intended to demonstrate to radiologists information management and radiological education using the power of computers.

Liz Beckmann

BIR Calendar

Unless otherwise indicated, enquiries about these events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-580 4085).

RADIOLOGY AND ONCOLOGY 91 and MED X RAY
29 April–1 May
Metropole Hotel, Brighton
Speakers:

3M Mayneord Memorial Lecture:
Prof. D. M. Goldenberg
Silvanus Thompson Memorial Lecture:
Dr R. Berry
Presidential Address:
Prof. C. A. Joslin
Mackenzie Davidson Memorial Lecture:
Prof. S. Dische

Radiation Oncology and Radiobiology: Particle Therapy
June 7, 1991
Organizer: Dr R. D. Errington
Speakers: Dr D. Bewley, Dr N. McNally, Prof. G. W. Griffin, Mr J. Hungerford, Dr T. Bates, Dr S. Gore and Prof. J. M. Slater

The New Legislation — Friend or Foe (After the White Paper ... and into Europe)
June 13, 1991
Scientific Lecture Theatre
All day meeting organized by the Industry Committee
Chairmen: Prof. C. A. Joslin, Dr O. Craig and Miss D. Rigg
Speakers include Dr J. Roylance, Dr I. Watt, Mr E. Sutherland, Prof. I. Isherwood, Mrs S. Williams and Mr P. Richardson

Conversazione
June 27, 1991
Painter's Hall, London
Lecture: "Half an Eye on the Sky", by Sir Stephen Furness.

MRI Meeting
October 16, 1991
Organizer: Professor B. S. Worthington

Brachytherapy – The past, present and future
October 23 and 24, 1991
Institution of Electrical Engineers
(Meeting to be held in association with Nucletron Ltd)

Hypoxic cell sensitizers: do they have a future?
November 15, 1991
Organizer: Dr R. Camplejohn

Radiosensitivity
February 11, 1992
Joint BIR/RCR meeting

Industry News

MED X RAY – Brighton

> Hopefully the attractions at the exhibition this year will be more than enough to lure delegates away from the delights of sea, sun, sand and Brighton rock.

ICL *(Stand 74)* will be displaying a Medical Portfolio Radiology Management system . This is a powerful integrated system designed to meet the needs of the modern radiology department in the Acute sector of healthcare including registrations, appointments, radiological reporting, film filing, and PAS linkage.

The computer aided diagnosis package is designed to help clinicians in the diagnosis of difficult conditions such as Acute Abdominal Pain and Inflamatory Bowel disorder. ICL will be demonstrating training packages for pre- and post-graduates.

For further information please visit Stand 74.

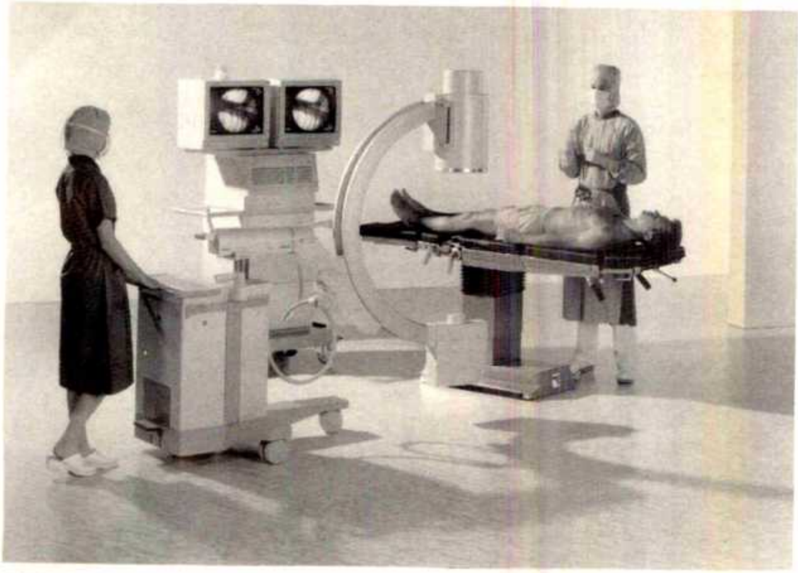
3M *(Stand 5)*. Taking pride of place on 3M's stand is their new Laser Imager XL System which sets the highest standards in medical imaging technology. The System is a multi-input, fully integrated unit suitable for departments wishing to connect several modalities simultaneously in both analogue and digital formats; MR, CT, DSA, ultrasound and digital radiography.

3M New Laser Imager "XL" System

Philips Medical Systems (*Stand 36*) will be demonstrating their new BV29 mobile and surgical interventional imaging system for the first time at MED X RAY. It features the award-winning C-arm and advanced digital processing facilities which provide excellent image quality and reduced X-ray dose.

Also on Philips' Stand will be a Critical Care Workstation, designed specifically to facilitate easy and immediate access to image and text information which can be sent automatically from the central management device to a user-specified Critical Care Workstation in any remote hospital area where vital clinical information is required.

For further information visit Stand 36 at Brighton.



Philips' BV29 Mobile Surgical and Interventional X-ray System

Siemens (*Stand 3*) is introducing two major additions to its range of diagnostic imaging systems this year. The "Somatom AR" for computed tomography and the "Magnetom P8" for magnetic resonance imaging are new concepts in terms of technology and space saving.

Also on Stand 3 will be the new "Polytron 1000S". Intended for digital angiography/DSA applications this equipment provides excellent image quality on a 1024 x 1024 matrix, storage capacity for up to 1000 images and a minimum frame-rate of 12 images-per-second.

The "Siremobil 4" X-ray equipment with laser targeting device and 100-frame subtraction memory is designed for use in operating theatres. The laser 'cross-hairs' and drill localization punch allow perfect alignment of plate holes and screws and reduce direct radiation exposure to the surgeon's hands.

The Company's technical support department will be demonstrating "OPSIS", a remote-diagnostic system for advanced medical equipment which allows specialist support to be obtained quickly and easily from Siemens' facilities in the UK and Germany. Product specialists will be available for the duration of the exhibition to assist with demonstrations and for informal discussions.

Guildford Magnetic Imaging Ltd (*Stand 73*) performs private and NHS MR scans. Visitors will be able to see an exhibition of the work undertaken in the clinic, together with videos showing some of the sequences performed routinely. Literature about their clinics will also be available.

Du Pont Diagnostic Imaging (*Stand 34*) have launched a major new telephone service for users of X-ray film and equipment, aimed at improving the efficiency of contact between the company and its customers. Directline offers a single point of contact within the company for orders and customer service, but also plays an active role in providing information on new technologies and products to both present and potential customers, whatever the size of hospital or geographic location. The Du Pont Directline already makes regular contact with over 450 customers.

Du Pont will also be showing a new Compact Daylight System that uses new, low-fume processing chemicals to improve the working environment. In addition the LINX Networking System and Laser Imager, aimed at improving productivity in busy Radiology departments, represents technology for the future. The System provides a flexible link between electronic imaging modalities and the Laser Imager.

For further information why not visit them on Stand 34 for a demonstration.

Diasonics Sonotron (*Stand 66*) is launching two new X-ray systems and two interventional surgical tables at the exhibition including the Series 9000 Mobile Image Intensifier. This is a multi-purpose, cost effective system providing a high-performance alternative to equivalent static units. Being modular in construction it allows for developments in technology to be incorporated.

For further information visit Diasonics on Stand 66

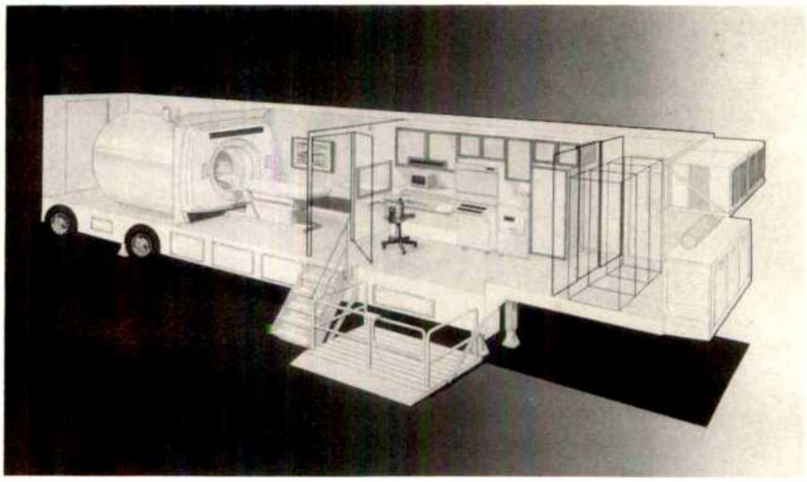
Fuji (*Stand 29*) will be showing visitors their latest development in Computed Radiography technology. The FCR AC-1 and AC-2 provide the two functions of image reading and image recording in one compact design. In addition the AC-2 has the revolutionary capability to transmit and receive a digitized signal so that images can be viewed and manipulated from any remote location.

For further information visit Fuji on Stand 29

Calumet *(Stand 61)* is one of the world's major suppliers of mobile medical units. Mobile diagnostics is already well established in the USA and, with increasing pressure on budgets and the high cost of building and operating conventional static diagnostic units, healthcare institutions in Europe are looking more to this solution.

Calumet has set up its European head offices in Camberley, Surrey. The Company is working alongside several Medical Service Companies enabling NHS and private hospitals to share mobile MRI units which would otherwise be beyond their means.

In the usual instance a Medical Service Company will buy and operate the unit so that the healthcare provider can contract only the services it requires.



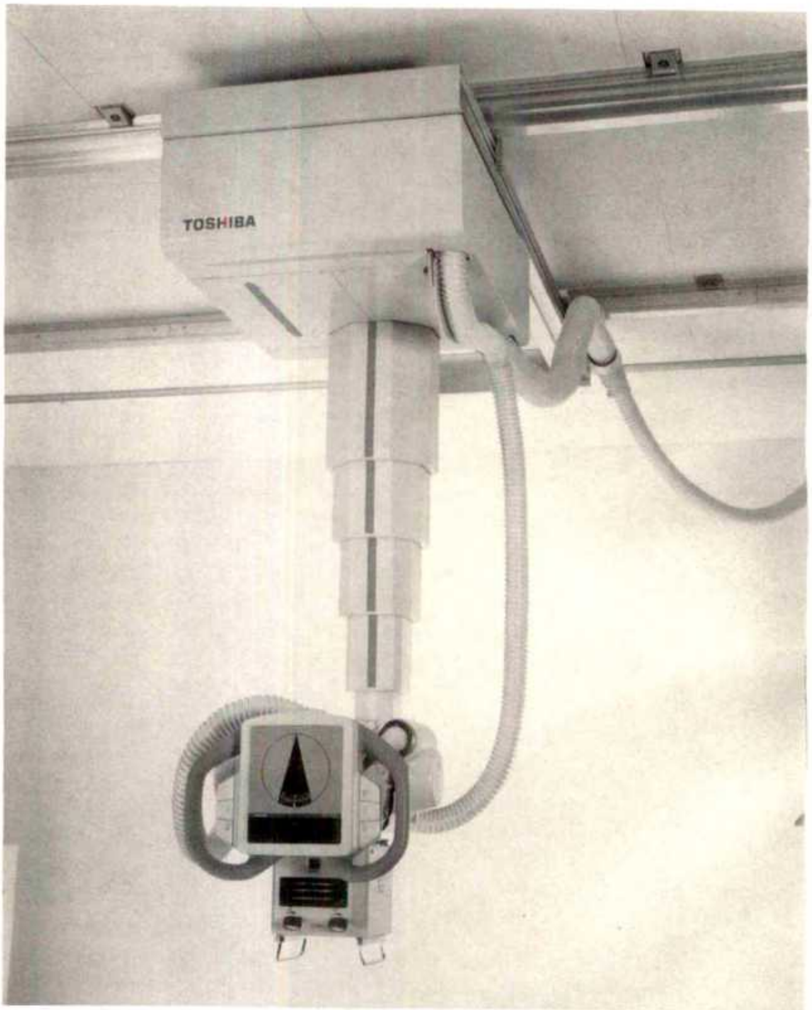
A Mobile Medical MRI Diagnotic Unit, equipped with a GE MR MAX Imaging centre. Interested parties should visit Calumet's Stand 61 at MED X RAY.

Grand Prix in Good Design for Toshiba

Toshiba's ceiling suspended X-ray tube support model DST-100A has been awarded the 1990 Good Design Grand Prix (G-mark) in the medical care, health and welfare field by the Japanese Ministry of International Trade and Industry.

The DST-100A is widely used for radiography and has an ergonomically-designed operation handle which can be rotated freely to facilitate positioning. The DST-100A can be operated intuitively since the colour assigned to each movement direction (X, Y and Z axis) matches the colour of the corresponding movement control switch on the handswitch panel.

For more information contact:
Mr H de Gier, Product Manager
X-Ray, Toshiba Medical Systems
Europe BV, Schieweg 1,2627 AN
Delft, The Netherlands
Tel. 31 15 610121,
Fax 31 15 622359



X-ray tube support system model DST-100A from Toshiba

Simis Medical Imaging

(*Stand 76*) will be showing their latest range of low cost CT/MRI data transfer systems and remote diagnostic consoles as well as their X-ray image archiving and archiving systems for realtime ultrasound studies. These systems incorporate the latest in digitisers including a 2 mega-pixel version for transfer of ultra high resolution studies.

All SMI's products are programmed in C running under UNIX or MS-DOS and fully exploit the multi-tasking window managed environment used. Examples of their products will be seen running on SUN workstations IBM PC's and Apple Macintosh as well as the latest RISC based Acorn Archimedes 540 system.

SMI also offer consultancy services to the medical imaging industry providing quick, low cost solutions to a wide range of problems from simple enhancements to local and wide area networks. This service is equally available to hospitals or institutions with a need for low cost one off solutions.

Linear X-ray detector for NDT

Linear X-ray detectors from Thomson Tubes Electroniques give direct digital outputs for data processing and are ideal for high-speed radiological scanning in non-destructive testing. The detectors may be used for materials inspection with automatic signal processng.

The THX 2024 detector array is supplied in 512 and 1042 element versions. The pitch is 0.45 mm giving corresponding sensitive lengths of 230 mm and 460 mm. The minimum integration time per line is 1.5 ms which makes scanning speeds of up to 60 cm/s possible for the 512-element version and 30 cm/s for the 1024-element version. The THX 2024 includes a separate preprocessing unit which drives the detector and carries out gain and offset corrections. The output is in 8-bit TTL symmetric pairs. The unit operates with an X-ray energy range between 20 kVp and 160 kVP.

For further information please ring: (33-1) 49 09 28 28

Meadox (UK) Ltd — Company Profile

Meadox (UK) Ltd was established in 1978 as the UK distribution outlet for Meadox Medicals Inc., a multinational corporation based in New Jersey, USA.

For over 30 years Meadox Medicals Inc. has pioneered the development of vascular implants and has representation and distribution in over 90 countries. An important recent addition to the group has been Surgimed A/S, now known as Meadox Surgimed A/S, based in Copenhagen, Denmark. As leaders in the development and manufacture of angiography products, and in particular balloon catheters used in angioplasty, the acquisition of Surgimed has been a logical step in the growth of a company committed to the treatment of vascular disease.

Although a wholly owned subsidiary, Meadox (UK) Ltd functions as an independent autonomous company managed and staffed entirely with British personnel. Our current seven figure sales turnover has been achieved by an annual average growth of 15% since 1986 and we expect to continue to expand at that rate.

Customers

We are selling successfully to all major vascular disease centres in the UK where our thrust is towards vascular surgeons and interventional radiologists. Our product range also brings us into contact with general surgeons, cardiologists, cardiac-surgeons, oncologists, urologists, gastroenterologists and all relevant nursing staff.

People

The Meadox (UK) Ltd sales force consists of 10 highly trained representatives covering the whole of mainland Britain with a regional and national management structure. Our representatives, the majority of whom come from a nursing background, are trained in the application and use of all our product lines and invariably call on more than one department on each hospital sales call.

Our policy of maintaining a highly efficient motivated sales team, together with an in-house administrative, marketing and customer service team, has enabled Meadox (UK) Ltd to penetrate new markets and successfully maximize market share by building very close links with all the leading innovators in the field. A key to our success is a committment to added value and service where educational support and sponsorship feature strongly in our sales strategy. Included in the Meadox (UK) Ltd team are specialists in regulatory affairs and clinical trail management whose experiences in new product introduction proves invaluable.

Our centrally located Dunstable warehouse is proud of its dispatch record, where our fully computerized order processing, stock, and batch recall systems enable 97% of orders received to be shipped that same day.

Company Profiles

We hope that the Company profile will become a regular and useful feature in the BIR Bulletin.

Upon enrolling in the Company Subscriber Scheme member companies are asked to submit a short profile of the company, about 300–500 words long.

All existing members are invited to submit a profile for publication subject to editorial discretion.

Further details on the Company Subscriber Scheme in general and on Company Profiles in particular may be obtained from Tony Hudson at the BIR. Tel: 071-580 4085 or Fax: 071-255 3209.

BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £275 p.a. member companies are offered an attractive benefits package.

To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex
TW8 9AX. Tel. 081-560 2131.
Product Areas 1.
Contact Mr G. Mountford, Director.

American Medical Ltd
PO Box 971, London SW10.
Tel. 071-352 8051. Fax: 071-376 4508.
Product areas 1, 3, 4, 5, 7, 8.
Contact Betsy Riley, Managing Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury, Bucks HP20 2TP. Tel. 0296 395222.
Product areas 4, 5, 6.
Contact Mr James McLaughlin, Sales and Marketing Manager.

Bard Ltd
Forest Houe, Brighton Road, Crawley, West Sussex RH 11 9BP.
Tel. 0293 27888, ext. 2204.
Product area 2.
Contact Peter Dekkers, Product Manager.

British Nuclear Fuels plc
Room 525, Hinton House, Risley, Warrington, Cheshire WA3 6AS.
Tel. 0925 835022.
Product areas 8, 11.
Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Bruel & Kjaer (UK) Ltd
92 Uxbridge Road, Harrow, Middlesex, HA3 6BZ. Tel. 081-954 2366.
Product areas 3, 6.
Contatct Mr D. Lewis, Sales Manager.

Calumet Coach Co.
33 Shallbourne Rise, Camberley GU1J 2EJ. Tel. 0276 64490.
Product areas: 1, 4, 5.
Contact Mr P. Supple, Managing Director of International Operations.

Cardiac Services Ltd
95A Finaghy Road, South Belfast
BT10 OBY. Tel. 0232-625566.
Product areas 1, 3, 4, 5, 6.
Contact Mr R. J. Brown. Managing Director.

Cea (UK) Ltd
Nissen House, Grovesbury Road, Leighton Buzzard, Bedfordshire
LU7 8SS.
Tel. 0525 382529. Fax: 0525 372619.
Product areas 1, 3, 4, 5, 6.
Contact John Dunster, Managing Director.

Clinical Press Ltd
Redland Green Farm, Redland, Bristol BS8 7HF. Tel. 0272 420526.
Product area 17.
Contact Dr Paul Goddard, Chairman.

Data-Med Computer Services Ltd
10 Faraday Building, Highfields Science Park, University Boulevard, Nottingham
NG7 2QP.
Tel. 0602 431431. Fax: 0602 430782.
Product area 13.
Contact Mr C. Fields, Sales Manager.

Du Pont (UK) Ltd
Wedgwood Way, Stevenage, Hertfordshire SG1 4QN.
Tel. 0438 734000.
Product areas 1, 3, 4, 5, 6, 7, 9 and 10.
Contact Mr E. G. Lovat, Product Manager, Diagnostic Imaging.

E. G. & G. Limited
Vale Road, Windsor, Berkshire SL4 5JP.
Tel. 0753 855611.
Product areas 1, 6, 7, 8.
Contact Mr Roy Hauton, Sales Executive (Therapy).

Elscint (GB) Ltd
Colonial Business Park, Colonial Way, Watford, Herts WD2 4PT.
Tel. 0923 39511.
Product areas 1, 3, 4.
Contact Faith Gorman, Marketing Manager.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20.
Tel. 081-446 9714.
Product areas 1, 2, 8.
Contact Richard Bayliss, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London
NW3 6JH. Tel. 071-586 9351.
Product areas 1, 3.
Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
34 Shakespeare Street, Nottingham
NG1 4FQ. Tel. 0602 483807.
Product areas 1, 3, 4, 5, 6.
Contact Miss Eileen Parr, Commercial Manager.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks SL1 4ER. Tel. 0753 874000.
Product areas 1, 2, 3, 4, 5, 6, 8, 9.
Contact Jill Mitchell, UK Sales Support.

Kodak Ltd
PO Box 66, Station Road, Hemel Hempstead, Herts HP1 1JU.
Tel. 0442 61122.
Product area 1.
Contact Mr P. E. Blackwell, Manager, Health Sciences Division.

Lanmark
PO Box 317, Beaconsfield, Bucks
HP9 2LR. Tel. 0494 791615/670586.
Product areas 1, 3, 4, 5, 9, 10, 15, 16.
Contact Liz Beckmann, Director.

3M UK PLC
3M House, Bracknell, PO Box 1,
Berks RG12 1JU. Tel. 0344 426726.
Product area 1.
Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney, Northampton NN3 4RQ. Tel. 0604-46132.
Product areas 4, 5.
Contact Mr D. G. L. Wood, Business Manager.

M. A. S. Medical Ltd
Armytage Road, Brighouse, West Yorkshire HD6 1QF. Tel. 0484 721906.
Contact Martin York, Managing Director.

Meadox (UK) Ltd
Matthew House, Matthew Street, Dunstable LU6 1SD. Tel. 0582 605111.
Product area 2.
Contact Mrs Sheila Heap, Sales and Marketing Manager.

Medical Xray Supplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU. Tel. 081-205 9500.
Product area 1.
Contact Mr R. J. Laird, Sales Director/Mr K. Wartnaby, Managing Director.

Mitsubishi Electric UK Ltd
Travellers Lane, Hatfield, Herts AL10 8XB.
Tel. 07072 78756.
Product area 14.
Contact T. F. McCloud, Sales and Marketing Manager.

National Power plc
14 Newgate Street, London EC1A 7AM.
Tel: 071-634 6898.
Product areas 7, 8.
Contact Mr A. J. Swanson, Assistant Company Secretary.

Nuclear Associates
100 Voice Road, Carle Place, New York 11514-1593, USA. Tel. 516-741 7614.
Product areas 1, 3, 4, 5, 6, 8.
Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd
Nucletron House, Tarporley Business Centre, Tarporley, Cheshire, CW6 9UY.
Tel: 0829 733611.
Product areas 6, 8.
Contact Mrs Marilyn A. Hart, Office Manager.

Nycomed (UK) Ltd
Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA.
Tel. 021-742 2444.
Product areas 1, 3.
Contact Mr L. Birch Hansen, Managing Director.

Oxford Magnet Technology
Wharf Road, Eynsham, Oxford.
Tel. 0865 880880.
Product area 1.
Contact Pauline Hobday, Director of Sales and Marketing.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ.
Tel. 081-741 1666.
Product areas 1, 3–8.
Contact J. M. Woolston, Sales and Marketing Manager.

Polaroid (UK) Ltd
Ashley Road, St Albans, Herts AL1 5PR.
Tel. 0727 59191.
Product areas 1, 3.
Contact David Hollingworth, Marketing Manager.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 ODR.
Tel. 09277-67433/63320.
Product area 8.
Contact Mr R. K. Beach, Director.

Quantel Ltd
Administration Centre, Kiln Road, Newbury, Berkshire RG13 2HA.
Tel. 0444 232323.
Product areas 2, 10.
Contact Mr Christopher Trim, Publicity Officer.

Radiological Protection Services Ltd
61 Lind Road, Sutton, Surrey SM1 4PP.
Tel. 081-643 6374.
Product area 8.
Contact B. H. Cutting, Managing Director.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex RH15 9NE. Tel. 0444 232323.
Product areas 1, 2, 3.
Contact Mr Simon Higginbotham or Mr S. Hearne, Product Managers.

Siemens plc
Siemens House, Windmill Road, Sunbury on Thames, Midlesex. Tel. 0932 752334.
Product areas: 1, 2, 3, 4, 6, 8, 9, 10, 13, 14, 15.
Contact L. J. McFadyen, Marketing Assistant.

Sony (UK) Ltd
Jays Close, Viables, Basingstoke, Hants RG22 4SB. Tel. 0256 483564.
Product area 14.
Contact Richard Holt, Marketing Manager.

Toshiba Medical Systems UK
Manor Court, Manor Royal, Crawley, West Sussex RH10 2PY. Tel. 0293 560772.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr S. M. Weeden, Manager X-ray Products.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands. Tel. 015 61 0121.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr P Blonk, Office Manager, X-ray BU.

Vertec Scientific Ltd
5 Comet House, Calleva Park Estate, Aldermaston, Reading RG7 4QW.
Contact Mr Frans Verlaan, Managing Director

Wardray Products Ltd
Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP.
Tel. 081-398 9911.
Product area 8.
Contact Mr R. B. Wardley, Managing Director.

William Cook (Eur) Ltd
6 Such Close, Letchworth, Hertfordshire SG6 1JF. Tel. 0462 482884 Fax: 0462 480944.
Product area 2.
Contact Tessa Phizacklea, Product Manager.

X-rite (H. Miller Graphics Ltd)
8 Moody Street, Congleton, Cheshire CW12 4AP. Tel. 0260 279988.
Product areas 1, 12.
Contact Mrs P. Dhanani, Medical Sales.

KEY TO PRODUCT/ SERVICE AREAS

1: Diagnostic X-ray including NMR and CT
2: Interventional radiology
3: Ultrasound
4: Nuclear medicine
5: Radiopharmaceuticals
6: Radiotherapy and oncology
7: Radiobiology
8: Radiation protection
9: PACS
10: Image processing
11: Nuclear fuel cycle services
12: Quality assurance.
13. Radiology data management computer systems
14. Video printing
15. Equipment leasing
16. Hospital-shared services
17. Medical Publishing

Meetings and Courses

G.R.A.D.O.4, International Meeting on Oncologic Imaging on Endocrine Glands Tumours
May 9-10, 1991
Rome, Italy
Further details: Luigi Tipaldi, Istituto Regina Elena, Radiologia e diagnostica per immagini, Viale Regina Elena, 291 00161 Roma, Italia. Tel: (06) 4985207. Fax: (06) 4452337.

Skin Dosimetry: Radiological Protection Aspects of Skin Irradiation
May 13–15, 1991
Dublin, Ireland
Further details: Commission of the European Communities, DG X11/D/3, rue de la Loi 200, B-1049, Brussels.

Joint Meeting of the Cardiovascular and Interventional Radiological Society of Europe
May 13–16, 1991
Oslo, Norway
Further details: Medical Congress Management, PO Box 2, CH-8029, Zurich, Switzerland. Tel: (01) 255 19 15. Fax: (01) 261 05 78.

Contrast-Enhanced Magnetic Resonance
May 23–25, 1991
California, USA
Further details: Society of Magnetic Resonance in Medicine, 1918 University Avenue, Suite 3C, Berkeley, CA 94704, USA. Tel: (415) 841-1899. Fax: (415) 841-2340.

Gaia European Overview on Ultrasound from Diagnosis and Intervention to Treatment
May 31–June 2, 1991
Vila Nova Gaia, Portugal
Further details: Ms Anabela Menezes, Dept of Imagiology and Interventional Radiology, Santos Silva Hospital, 4400 Vila Nova Gaia, Portugal. Tel: 782 0418.

33rd Annual Meeting of the International College of Angiology
June, 1991
Singapore
Further details: Denise M. Rossignol, International College of Angiology, 1044 Northern Boulevard, Ste. 103, Roslyn, New York 11576, USA. Tel: (516) 484-6880. Fax: (516) 625-1174.

Abdominal Ultrasound Imaging, Hands-on Instruction
June 10–14, 1991
Texas, USA
Further details: Keith Mauney & Associates Inc., 600 East Las Colinas Boulevard, Suite 250, Irving, TX 75039 USA. Tel: (214) 402 8250.

Obstetric/Pelvic Imaging, Hands-on Instruction
June 17–21, 1991
Texas, USA
Further details: Keith Mauney & Associates Inc., 600 East Las Colinas Boulevard, Suite 250, Irving, TX 75039 USA. Tel: (214) 402 8250.

10th International Conference on Laser Spectroscopy
June 17–21, 1991
Font-Romeu, France
Further details: Professor M. Ducloy, Laboratoire de Physique des Lasers, Universite Paris-Nord, F-93430 Villetaneuse, France.

The Leeds Gastroenterology Course for Radiologists
July 1–5, 1991
Leeds
Further details: Miss Pat Kentley, Level 7, Worsley Medical Building, University of Leeds, Leeds LS2 9JT.

EuroPACS 91
July 2–3, 1991
Berlin, Germay
Further details: Professor Heinz U. Lemke, c/o University Klinikum Rudolf Virchow - Wedding, Altes Rontgenhaus-Raum 1005, Augustenburger Platz 1, D-1000 Berlin 65.

Second European Summer School on Radiological Protection
July 8–12, 1991
Cambridge
Further details: Liz Hide, IBC Technical Services Ltd, Bath House (3rd Floor), 56 Holborn Viaduct, London EC1A 2EX. Tel: 071-236 4080. Fax: 071-489 0849.

The 14th Annual Conference of the Australasian College of Physical Scientists in Medicine
July 22–25, 1991
Sydney, Australia
Further details: Secretariat EPSM 91 Conference, The IPACE Institute, Box 1 PO, Kensington, 2033, Australia.
Tel: 02 6973178; Fax: 02 662 6983.

The 2nd International Conference of the Kenya Association of Radiologists
August 7–9, 1991
Nairobi, Kenya
Further details: Dr J. K. Kitonyi, Conference Secretary, Dept of Diagnostic Radiology, University of Nairobi, PO Box 19676, Nairobi, Kenya. Tel: 724722. Fax: 340969.

Tenth Annual Scientific Meeting and Exhibition
August 10–16, 1991
California, USA
Futher details: SMRM Business Office, 1918 University Avenue, Suite 3C, Berkeley, CA 94704, USA. Tel: (415) 841 1899. Fax: (415) 841 2340.

The Bart's/London FRCR II Revision Course
August 27–29, 1991
London
Further details: Mrs C. Burrage, Course Secretary, Room 26, Dunn Laboratories, St Bartholomew's Hospital, London EC1A 7BE. Tel: 071-601 7531. Fax: 071-607 7024.

Paediatric Radiology Course
September 5–6, 1991
Sheffield
Further details: Dr G. M. Steiner, Consultant Radiologist, Children's Hospital, Western Bank, Sheffield S10 2TH. Tel: 0742 761111.

The Cyto-Histologic Diagnosis of the Microcalcifications - Screening and Calcic Signal
October 11, 1991
France
Further details: M. J. Rodiere, Institut D'Imagerie Medicale, Miniparc - Bat 2, Rue de la Croix Verte, 34090 Montpellier, France.

1st Congress of the World Federation of Interventional and Therapeutic Neuroradiology
October 11–13, 1991
Zurich, Switzerland
Further details: Medical Congress Management, PO Box 2, CH-8029, Zurich, Switzerland. Tel: (01) 255 19 15. Fax: (01) 261 05 78.

6th Symposium Mammographicum
April, 1–3, 1992
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London, W1N 3DG.
Tel: 071-636 4430. Fax: 071-323 3100.

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Assurance of Quality in the Diagnostic X-Ray Department

The report of the BIR Diagnostic Methods Committee

Editors

J A Garrett, Director of Medical Equipment Management Organisation, Bristol & Weston Heath Authority, UK
D Gifford, Deputy Chief Physicist, Frenchay & Southmead Health Authorities, UK
M J Harvey, Middlesex Hospital, London, UK
P Goddard, Consultant Radiologist, Bristol Royal Infirmary, UK

Producing images, whether photographically or in electronic form, is the primary purpose of the diagnostic radiology department.

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The second section of the book presents the wider systems approach to quality assurance with reference to recent standards for QA and how these may be applied to diagnostic radiology.

The final part discusses quality assurance in computer assisted imaging, computed tomography, magnetic resonance imaging, and digital subtraction angiography.

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OPTIMIZATION OF IMAGE QUALITY AND PATIENT EXPOSURE IN DIAGNOSTIC RADIOLOGY

(BIR Report 20)

Editors:

B M Moores, B F Wall, H Eriskat and H Schibilla.

Contents: Introduction. Image Perception. Physical Assessment of Image Quality. Clinical Assessment of Image Quality. Optimization of Image Quality and Patient Dose - Paediatric Radiology - Mammography - Chest Radiography - Technical Factors. Patient Dose Measurements and Quality Assurance. CEC Image Quality and Exposure Criteria Trial. Panel Discussions. Conclusions and Perspectives for Future Research. CEC Study Group Document on Quality Criteria for Diagnostic Radiographic Images.

Key components in quality assurance in diagnostic radiology are image quality and patient exposure. Quality criteria defining optimum procedures should ensure that the most accurate and reproducible diagnostic information is obtained from radiographs, but at the same time minimize exposure of the patient to ionizing radiation. Formulation of such criteria was the aim of a workshop organized jointly by the CEC and NRPB, of which this book is the edited proceedings. A revised list of quality criteria for common diagnostic examinations was drawn up by a CEC Study Group and is appended to the proceedings.

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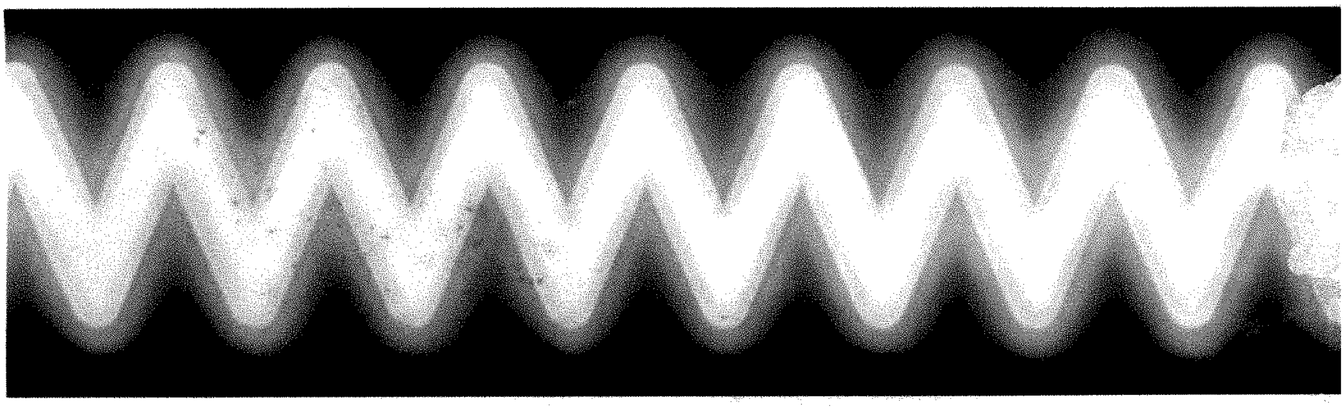

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(BIR Report 19)

Editor

N J McNally, Gray Laboratory, Mount Vernon Hospital, Middlesex

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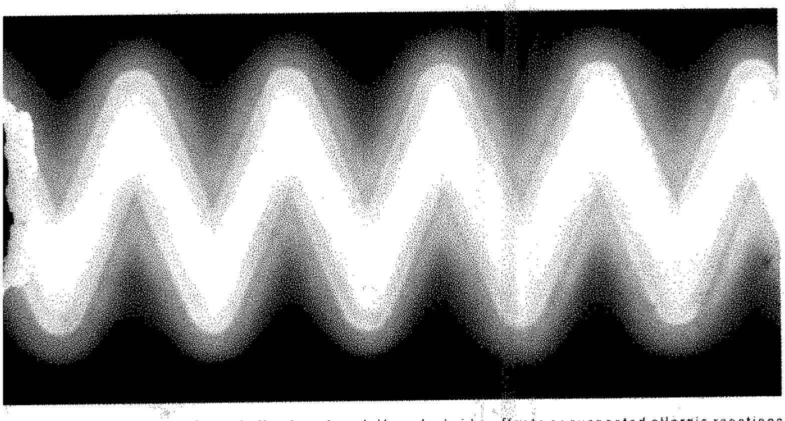

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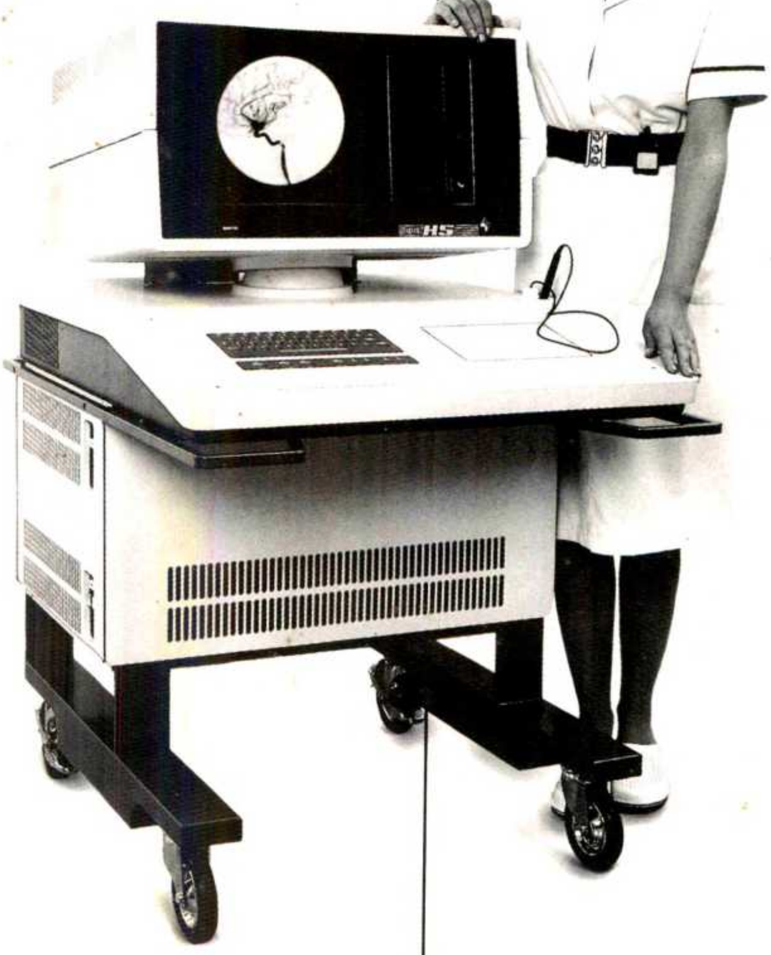

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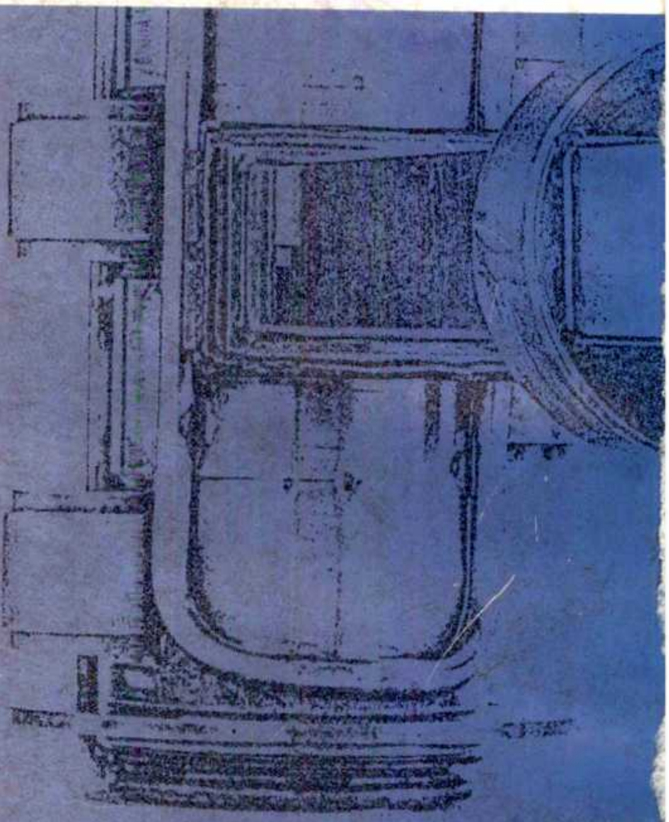

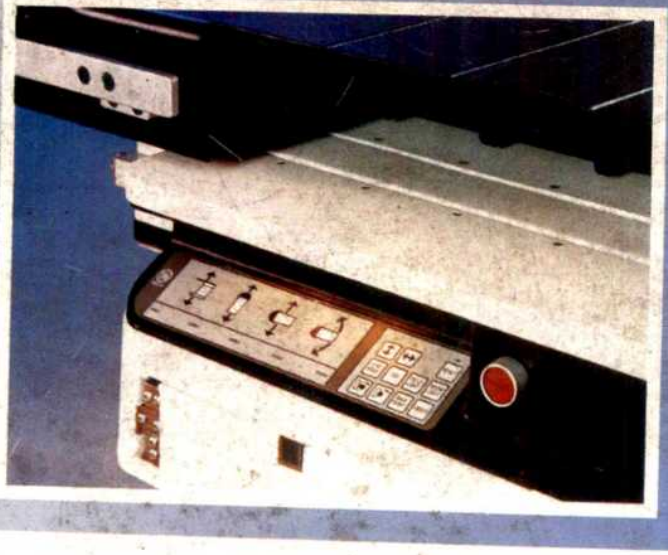

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